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January-February, 1945

Number 1

THE GROWTH AND DEVELOPMENT OF ALLERGY

A Ten-Year Study of One Hundred Allergic Children from Birth to Ten Years of Age

NORMAN W. CLEIN, M.D., F.A.C.A.
Seattle, Washington

WHAT happens to infants who exhibit allergic manifestations during the first few months of life? Do they develop other types of allergy as they grow older? Do they "outgrow" their allergic symptoms? When do these symptoms develop and what is the course of the allergic cycle in the growing child? Ten years ago in an article by the same author entitled "Allergy in Infants, the Significance of the First Allergic Manifestations," several statements were made. First was the fact that 80 per cent of allergic infants developed their first allergic symptoms or "shock" before they were four months old. Second, the conclusion of that article raised a question, namely—"As a result of these observations, I believe that the significance of diagnosing the first allergic manifestation in infancy is primarily that of recognizing the presence of an allergic state. Specific attention to the diet and environmental factors during childhood may prove to be important prophylactic measures in preventing or minimizing the major allergic diseases." This paper will attempt to answer this question.

The present study is a follow-up of 100 allergic infants over a period of from ten to fifteen years. All patients were seen in private practice from birth to the present. They were examined and treated regularly for routine preventive care as well as for acute illnesses. During this time it was my pleasure to know the child and his parents, and their reaction to his physical and mental problems. All examinations, diagnoses, treatments, records and conclusions were made by the author, so that this factor is common to all the patients over the entire period of this analysis. I was particularly interested in finding out what happens to these allergic

Presented at the First Annual Meeting of the American College of Allergists, Chicago, Illinois, June 10 and 11, 1944.

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people. If we feel that an infant is a potential candidate for hay fever, hives, or asthma, is it within the realm of our knowledge to do anything about it? Are specific prophylactic allergic measures begun early in life of any value in preventing major allergic disease? No attempt will be made to discuss methods of diagnosis or treatment, other than a few general conclusions presented by this study.

Two types of allergic symptoms will be discussed: (1) the early infant group consisting mainly of a rash, vomiting, and gastro-intestinal symptoms; (2) the major allergic diseases, namely perennial allergic rhinitis, pollen hay fever, asthma, eczema, hives, and gastro-intestinal symptoms.

It is significant to every pediatrician as well as those physicians who treat infants and children to know that approximately 82 per cent of the allergic babies develop their first allergic symptom by four months of age; 39 per cent have their first allergic shock by one month of age, and 24 per cent by two months. A few in this study (11 per cent) did not develop any allergic manifestation until they were between the ages of one and ten years. For practical purposes we may label most of these infants as "allergic" before they are four months old.

The early allergic manifestations are of three rather distinct types, several of which may occur in the same patient at the same time. These symptoms were considered allergic because they disappeared with the elimination of the offending allergen and reappeared when the causative food or other factor was added. The clinical trial verified the diagnosis.

The rash or eczema was present in fifty-three cases and was usually due to some food, especially orange juice. Vomiting, or pylorospasm, occurred in thirty-six cases. This symptom was usually due to orange or milk, and was relieved by the substitution of other foods. Gastro-intestinal allergy consisting of severe persistent colic, excessive gas, recurrent diarrhea or constipation, was present in twenty-three infants. Ten years ago when raw egg yolk was routinely added to the milk formula of all infants at one or two months of age, 90 per cent of the allergic babies receiving raw egg yolk developed a rash, pylorospasm, or gastro-intestinal distress as their first allergic symptom. In a similar nonallergic group of babies, there were no allergic symptoms from egg yolk. In the present series egg yolk was not added to the diet of allergic babies until one year of age. Orange juice was the single most important allergen producing the initial allergic sensitization or shock. Cod liver oil was an occasional factor but it is becoming less important as we use more of the natural concentrates and the synthetic vitamin D preparations.

In three cases each, the original allergic insult was one of the more serious types of allergy, such as asthma, perennial rhinitis, and pollen hay fever. The "allergic tongue" was the symptom first noted in three cases. This type of tongue lesion consists of "hive"-like bald areas, circinate, with slightly raised reddish borders usually on the edges or tip of the tongue. These symptoms are due to food allergy and are aggra-

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TABLE I. AGE OF DEVELOPMENT OF FIRST ALLERGIC SYMPTOM IN 100 INFANTS

Age	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6-12 mo.	1-2 yr.	2-6 yr.	6-10 yr.
No. of Cases	39	24	13	6	2	5	3	5	3

82 per cent developed first allergic symptom by 4 months of age.
89 per cent developed first allergic symptom by 1 year of age.

TABLE II. FIRST ALLERGIC SYMPTOM MANIFESTED BY CASES

RASH (Eczema).....	53
VOMITING (Pylorospasm).....	36
GASTRO-INTESTINAL DISTRESS (More or less persistent colic, gas, diarrhea, constipation).....	23
ASTHMA.....	3
ALLERGIC RHINITIS (Perennial).....	3
ALLERGIC TONGUE (Geographic).....	3
HAY FEVER (Pollen).....	3
HIVES.....	1

Several symptoms may occur in same patient at same time.

TABLE III. TYPE OF MAJOR ALLERGIC DISEASE DEVELOPING IN 100 PATIENTS OVER TEN-YEAR PERIOD

No Major Allergy Developed.....	2	<i>Analysis of Gastro-Intestinal Symptoms</i>	20
ALLERGIC RHINITIS (Perennial).....	59	ABDOMINAL PAIN (Severe-chronic-recurrent)...	7
HAY FEVER (Pollinosis).....	38	DIARRHEA.....	3
ASTHMA.....	26	ACIDOSIS (Cyclic Vomiting).....	2
ECZEMA.....	33	CLAY-COLORED STOOLS (Hepatitis).....	2
GASTRO-INTESTINAL.....	20	CANKER SORES.....	2
HIVES.....	10	PRURITUS ANI.....	2
SWELLING OF EYES.....	2	MUCOUS COLITIS.....	1
MIGRAINE.....	2	DUODENAL ULCER.....	1
ITCHING SKIN (Persistent).....	2		
CAROTINEMIA.....	8		
ALLERGIC TONGUE.....	7		
MERCURY SENSITIVITY (Ointment).....	1		

Several symptoms may occur in same patient

TABLE IV. RELATIONSHIP OF MAJOR ALLERGIC SYMPTOMS AND THEIR COMPLICATIONS TO EACH OTHER

Cases	Perennial Rhinitis		Hay Fever Pollens		Asthma		Eczema	
	No. Cases	%	No. Cases	%	No. Cases	%	No. Cases	%
Perennial Rhinitis	59	26	21	32	12	20	21	32
Hay Fever (Pollens)	38	21	55	17	9	24	12	32
Asthma	26	12	46	8	30	6	8	30
Eczema	33	21	65	12	32	8	24	7

TABLE V. CHILDREN HAVING ONLY ONE MAJOR ALLERGIC DISEASE, UNCOMPLICATED

PERENNIAL RHINITIS.....	26
HAY FEVER (Pollen).....	17
ASTHMA.....	6
ECZEMA.....	7
Total.....	56

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vated by tart or "acid" foods. In later years, these lesions assume the appearance of what is commonly known as the "geographic tongue."

It is amazing to note that only two of the 100 infants *did not develop any major allergic disease* to their present ages of ten and twelve years, respectively. It is equally shocking to realize the exceedingly high incidence of those developing the so-called major allergic symptoms. *Ninety-eight of 100 allergic infants developed major allergic symptoms* in their first ten years.

PERENNIAL ALLERGIC RHINITIS (THE ALLERGIC NOSE)

Perennial allergic rhinitis was the most prevalent type of major allergy, and included those patients that are bothered by a "stuffy nose." These patients are usually worse during the night, because most of their symptoms are due to inhalant allergens. A short time after the patient awakens in the morning these symptoms may disappear. They recur during the daytime if food allergy is also a factor. These symptoms are more common in the winter since the patient spends more time indoors. They may have an associated pollen allergy in the summer.

The child with frequently recurring colds, "who no sooner gets over one cold before he catches another," is usually of this type. A chronic runny nose, sniffles, and occasionally a night cough are present. A temperature rise is usually not present except with an associated infection. Fifty-nine patients (59 per cent of the entire group) had this symptom. Several or all types of allergy may occur in the same patient. In other words, of fifty-nine perennial rhinitis cases, one-half had rhinitis as the only symptom, one of every three of these patients also had hay fever or eczema, and one of every five had asthma.

HAY FEVER (POLLINOSIS)

Seasonal hay fever or pollinosis was present in thirty-eight of the 100 cases. It was second in frequency of occurrence. These patients were mainly grass-pollen sensitive and a few tree-pollen cases. Fall hay fever is not a problem as we do not have ragweed in the Pacific Northwest. Grass hay fever was the only allergic symptom present in seventeen children. One-half of the pollen hay fever group also had perennial rhinitis, one-third had an associated eczema, and one-fourth of the grass-pollen patients had asthma.

ASTHMA

Asthma occurred in twenty-six patients ranging from the age of one month to twelve years. It was the *only* major allergic symptom in 6 per cent of the entire series. The diagnosis was apparent by the typical physical findings, wheezing, and labored breathing. This symptom was complicated with perennial rhinitis in about one-half of the total asthmatics; with hay fever in one-third of the cases and with eczema in about one-third of the asthmatic children. There were very few cases of severe asthma,

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and it was extremely rare for any of these patients to require hospital treatment. The pre-asthmatic cough (Table VII) was present in some cases but did not always develop into asthmatic wheezing.

ECZEMA

The varied types of rashes classified as allergic eczema were found in thirty-three patients. Many of the rashes which occurred as the first allergic manifestation disappeared within a relatively short time due to omission of the causative food, contact, or inhalant. Those that remained or recurred and became chronic problems are included in this group. Two-thirds of this eczema group also had allergic rhinitis, one-third had pollen hay fever, and one-fourth had asthma as a complication or as an associated allergic symptom. Eczema was the only major allergic symptom in 7 per cent of the entire series of 100 children.

GASTRO-INTESTINAL

Symptoms referable to the gastro-intestinal tract were varied, but very definite. The most common complaint was abdominal pain. This was often severe, recurred frequently, and followed no definite pattern as to time, location, or duration of the pain. Physical and laboratory findings were usually normal. Recurrent diarrhea, often alternating with constipation, was present in three cases. Cyclic vomiting causing severe dehydration, recurring with an acute infection, was a serious problem in two children. Once the allergic factor was under control, these symptoms disappeared. Clay-colored stools with no jaundice, but with abdominal pain, was present in two patients due to definite food allergy. Canker sores are a fairly common occurrence, but not often as severe as in two of these children. Pruritus ani, causing great distress, due to citrus fruits, occurred in several children. One case each of mucous colitis and duodenal ulcer were relieved by allergic management. The gastro-intestinal symptoms would disappear when the offending food allergens were avoided, and recur when these were added to the diet.

HIVES

Ten cases of hives, including two of severe angioneurotic edema were encountered in this group.

Other symptoms observed were: swelling of the eyes in two patients; migraine, 2; persistent itching skin, 2; carotinemia, eight; allergic tongue, seven; and mercury sensitivity and petit mal epilepsy in one case each.

Apparently, the first allergic symptom, such as a rash or pylorospasm, does not influence or predetermine the type of major allergy that will develop in later years. For instance, an infant having an allergic rash as the first symptom does not necessarily develop eczema later; he may develop any type of allergy at any time. The chart shows that infants having an

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TABLE VI. DOES THE FIRST ALLERGIC SYMPTOM INFLUENCE OR DETERMINE THE TYPE OF MAJOR ALLERGY WHICH DEVELOPS LATER?

First allergic symptom	No of Cases	Subsequent major allergic disease					
		Eczema	Allergic Rhinitis	Hay Fever	Asthma	Gastro-Intestinal	Hives
Rash (Eczema)	53	22	31	18	15	6	4
Vomiting (Pylorospasm)	36	14	24	14	8	11	6
Gastro-Intestinal (gas, colic, diarrhea, constipation)	23	2	5	5	8	4	2

Approximately the same number of children developed perennial allergic rhinitis, hay fever or asthma, whether the first symptom was a rash or vomiting. A larger number of the original "vomitters" developed gastro-intestinal allergy or hives than the "rash" or "G.I." groups. Those with early gastro-intestinal symptoms developed fewer cases of hay fever or eczema than the other groups.

TABLE VII. AGES AT WHICH MAJOR ALLERGIC SYMPTOMS DEVELOP IN INFANTS HAVING EARLY ALLERGIC MANIFESTATIONS

Major Allergic symptoms	No. of Cases	Age in years									
		1	2	3	4	5	6	7	8	9	10
Allergic Rhinitis (Perennial-frequent colds)	59	13	10	8	10	3	4	5	4	1	1
Hay Fever (Pollen)	38	2	4	10	7	4	3	2	4	1	1
Asthma	26	7	4	2	2	4	4	2	1		
Eczema	33	23	4	3	1		2				
Hives	10	1	4	2			2	1			
Gastro-Intestinal (Abdominal pain-cankers-diarrhea-constipation-colitis-pruritis)	20		3	4	1	3	4		3	1	1
Migraine	2						1		1		
Allergic Cough (pre-asthmatic)	30	6	7	5	3	5	1	1	1	1	
Total		52	36	34	24	19	21	11	14	4	3

76 per cent of major allergy developed the first five years.

85 per cent of major allergy developed in the first six years.

Conclusion: Only a small percentage (15 per cent) developed major allergy after six years of age. Early diagnosis, prophylaxis, and treatment are of great importance in preventing the development of major allergy after six years of age.

TABLE VIII. CHRONOLOGICAL ORDER IN WHICH MAJOR ALLERGIC DISEASES DEVELOP IN THE GROWING CHILD

Major Allergic Symptoms	No. of Cases	Order of Appearance			
		1st	2nd	3rd	4th
Allergic Rhinitis (Perennial-frequent colds)	59	31	24	4	
Hay Fever (Pollen)	38	12	15	10	1
Asthma	26	10	6	7	3
Eczema	33	28	4		1
Hives	10		6	3	1
Gastro-Intestinal	20	10	4	4	2
Migraine	2		1	1	

Several diseases may occur in the same patient.

ECZEMA, when present, was usually the first major allergic symptom because it persisted from the onset of the first allergic "shock" in infancy (twenty-eight out of thirty-three cases).

ALLERGIC RHINITIS (frequent colds) developed earlier and more frequently as the first major allergic symptom (53 per cent). This most common allergic symptom followed eczema, asthma, and other GI allergic diseases as the second type of allergic manifestation (40 per cent) in this cycle.

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initial rash or vomiting later developed allergic rhinitis, hay fever, or asthma in about the same proportion. Those that had pylorospasm in infancy developed more gastro-intestinal allergy and hives than the other two groups. Those with early gastro-intestinal symptoms had less chance of developing eczema as they grew older.

The age at which these infants and children developed their major allergic diseases is interesting because they occurred much earlier than commonly recognized. These figures are based on the age when the particular symptom was first diagnosed. There were more eczema cases in the first year as these were mainly infants in which the rash persisted and became chronic. Of the major allergic symptoms 76 per cent were diagnosed in the first five years and 85 per cent in the first six years. This means that most of our major allergic symptoms in children are pre-school-age problems. It is possible and probable that the early diagnosis and treatment were of great importance in preventing these diseases from becoming more severe, more complicated and more difficult therapeutic problems during the school age. The results of the prophylactic and active treatment of these "virgin" allergic cases appears to be more effective, rapid, and thorough, and there is less tendency for recurrence than in other groups of allergic children treated for the first time only after their major allergic disease had been well developed.

Pollen hay fever occurred more frequently in the three- and four-year-old group. These symptoms occur clinically in a mild form in many children, although the skin tests are frequently negative during the first few years. The nasal secretions often reveal an increased eosinophilia which is diagnostic. This is also true in most patients with the perennial type of allergic rhinitis.

There is not much regularity in the chronological order in which the major allergic diseases develop in the allergic cycle that occurs from infancy to adolescence. Perennial rhinitis was more often the first major symptom following the initial allergic shock in infancy. Thirty-one cases developed first in this group; twenty-four cases developed second, that is, after asthma, eczema or hay fever was already present; four cases occurred only after two other allergic symptoms had developed.

Pollen hay fever usually followed the perennial type of allergic rhinitis in this cycle of development. Two-thirds of the cases of hay fever developed as the second or third symptom in this chronologic lineup. In twelve patients, pollen hay fever was the first symptom of major allergy. Asthma was the first major allergic disease in ten cases. This is significant inasmuch as asthma is often considered the final development in the allergic cycle, instead of the first. The remaining types of allergy were about equally divided as to whether they happened to be the first, second, or third phase in the pathogenesis of major allergic disease.

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RESULTS OF TREATMENT

A short discussion of the results of treatment will be mentioned. Treatment was of the pediatric allergic type. These patients were considered primarily as a pediatric problem requiring the use of allergic methods of diagnosis and treatment. More chronic allergic disease in children has been unrecognized than any other type of illness. In many cases, if the diagnosis is made, treatment is inadequate. The most grateful parents are those whose allergic children have been successfully treated and relieved by allergic methods. These children had been treated with vitamins, cold shots, light treatments, tonics, change of climate, autogenous vaccines, and tonsil and adenoid operations, without any previous relief.

Treatment consisted of elimination, substitution, and avoidance of irritating factors such as foods, inhalants and contact substances. Since the infant is exposed to fewer foods and perhaps fewer external or inhalant factors than the adult, the diagnosis and treatment of his "virgin" allergic problems is often simplified. Fifty-three children required testing when other methods were unsuccessful. Twenty-eight were given desensitization treatments with specially prepared individual antigens, consisting of inhalants such as pollens, epidermals, dust, and molds.

The present health of these children, in a general way, is about the same as that for any other equivalent group of children physically and mentally. The results of treatment were as follows:

Excellent results (no symptoms).....	73
Good results	16
Fair or not much improved.....	11

Fifty-three remained clinically normal if they observed their diet schedule. Forty-two were well if they avoided the environmental factors that bothered them and in some cases continued to receive their specific antigen. Fifteen were normal on an unrestricted diet and without observing any special environmental rules.

The co-operation of the parent naturally has a great deal to do with our final results. It is much more difficult to control the diet, rest and environment of a child than that of an adult. After many years of contact with these parents and the children, their co-operation was appraised as "good" in fifty-five cases, "fair" in thirty-five and "poor" in ten. In other words, in almost 50 per cent of the cases we had little help from the parent. This means that many important prophylactic measures were never carried out and that our chances of success were only about 50 per cent of what they should be even with the best treatment. Of these cases, 76 per cent were treated early when the diagnosis was first made; that is, they were tested, treated, given antigen when necessary, and the application of other

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standard measures. The remaining 24 per cent were treated only after the major allergic symptoms recurred or became annoying or more serious. We cannot expect as good results from treatment of a "full-grown" disease as we can from an early case.

The present health status of allergic children depends not only on our accepted methods of diagnosis and treatment, but equally on the co-operation of the parent, the time of starting and continuing treatment, and the opportunity for occasional consultations with the well child and his parents. The attitude and co-operation of the child depend a great deal on that of his parents.

The tonsil and adenoid question is always important. Sixty-one children had their tonsils and adenoids removed. The indications were the same as those for children who are not allergic. The general health of the allergic child was improved in this manner. The allergic problem was always treated first, then surgery was performed if the symptoms still warranted this method of treatment.

COMMENT

The foregoing discussion has shown that practically *all allergic* infants develop major allergic disease or symptoms as they grow older. The standard accepted prophylactic measures failed to prevent these symptoms. Rigid dietary restrictions and specific environmental control factors begun in infancy, even when carried out faithfully and with excellent co-operation, did not prevent the development of hay fever, asthma, and other major allergies. There is no question that the symptoms were usually milder, reacted more readily to treatment and that there were fewer and milder recurrences. This adds up to the fact that proper treatment means fewer sick days, fewer days out of school, more active exercise and engagement in life's daily routine for these children. Since children play in "high gear" most of the time, this is quite important.

Ten years ago, when egg yolk was eliminated from our infant feeding formulae, the number of early allergic symptoms dropped appreciably; eighty-five of the 100 allergic infants in the original series ten years ago had a rash or eczema. When egg yolk was discontinued, the next group of 100 allergic infants had a rash in only fifty-three cases. This is a reduction of about one-third, meaning that fewer babies were given their first allergic sensitization. Since orange juice is also such a constant sensitizing food, we have eliminated this in any baby who has a family history of allergy or whose brothers or sisters have allergic problems. This has considerably reduced the initial allergic factors by about another one-third. Synthetic Vitamin C or other natural foods rich in Vitamin C such as banana, furnish adequate requirements of this vitamin. Of equal importance is a dust-free nursery for the infant, as inhalant factors are much more important than commonly considered.

If we cannot prevent allergy, have we been able to conquer its symptoms? Of these children, 76 per cent developed their major allergic prob-

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lems before school age. Only 15 per cent developed major allergy after six years of age. It was formerly believed that most asthma and hay fever developed in the pre-adolescent age. This was probably due to the fact that frequently medical care was not sought until the condition became serious enough to consult a physician. This suggests that the early diagnosis, prophylactic, and active treatment relieved the first symptoms sufficiently so that there were fewer remissions. Those that did recur were usually much easier to control.

Another important observation was that the treated allergic children "went through" measles, pertussis, and other severe infections without any more trouble than nonallergic children. Many textbooks claim 20 to 40 per cent of asthma in children develops after the acute infections. This is probably true in allergic children that have not had the benefit of prophylactic and active treatment. In this type of case, latent or potential allergy flares up as the result of the severe stress and strain of the infection.

SUMMARY

1. One hundred children having allergic manifestations in infancy were observed for at least ten years. Their first allergic symptoms usually occurred in the first four months of life, and were present as a rash or eczema, vomiting or pylorospasm, and gastro-intestinal distress such as colic, excess gas, diarrhea and constipation. Egg yolk and orange juice were the most common allergens in infancy.

2. When these infants were labeled "allergic," prophylactic dietary and environmental treatment was instituted and was stressed repeatedly at each examination.

3. Ninety-eight per cent of the allergic infants developed major allergic symptoms during the course of this observation in spite of early diagnosis and prophylactic treatment. These allergic diseases were of varied nature; perennial allergic rhinitis was most frequent, followed by hay fever (pollinosis), asthma, eczema, gastro-intestinal allergy, hives, and a few other less common conditions. Several of the above were often associated at one time or another in the allergic cycle in the child.

4. Only one allergic symptom in a child occurred in 56 per cent of the cases. Perennial rhinitis was the only major allergic symptom in 26 per cent, pollen hay fever in 17 per cent, asthma in 6 per cent, and eczema in 7 per cent. Other children had multiple symptoms.

5. The first allergic symptom in infancy does not usually determine the type of allergy that will develop later.

6. Most cases of major allergy developed before six years of age; only 15 per cent in this series occurred after six years of age.

7. Perennial allergic rhinitis occurred most often as the first major allergic symptom. Hay fever, asthma, hives, and gastro-intestinal symptoms develop as the first form of allergy more often than is generally recognized.

8. Prophylactic treatment, advocated early and thoroughly, did not pre-

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vent the development of major allergy as the child grew older. Ninety-eight of 100 children developed symptoms of major allergy. The preventive treatment probably minimized the course of the disease and its complications. Children adequately treated for allergic disease grow and develop physically the same as normal children.

9. Treatment was that of the pediatric allergist. The child was treated primarily as a pediatric problem with the aid and refinements of allergic technique.

CONCLUSION

This ten-year study has shown that with our present knowledge we cannot prevent the development of major allergic disease in infants who have an inherent allergic constitution. It is discouraging to know that, although we are able to diagnose the allergic state in the first few months of life, the infant will almost inevitably develop major allergic symptoms in his early childhood. Prophylactic treatment, in its present state of development, will probably minimize or ameliorate the allergic symptoms, allowing the child to grow and develop normally, both physically and mentally.

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MYOCARDITIS IN BRONCHIECTASIS. Saphir, Otto: *Arch. Int. Med.*, 72: 775, (Dec.) 1943.

It is noted that myocarditis is associated relatively more frequently with bronchiectasis than with uncomplicated pneumonia. Clinical data on eight patients (among 152) with bronchiectasis and associated myocarditis are presented. The most significant clinical observation is the discrepancy between the relatively slight elevation of temperature and the high pulse rate. At autopsy, two patients had hearts of normal size, six presented right ventricle hypertrophy. The myocarditis was diagnosed not by gross examination but histologically. There was recent myocarditis in five cases, subacute and chronic in one each. The cause of myocarditis very likely was a primary focus of bronchiectatic infection. It is suggested that a careful study of the myocardium in bronchiectasis and bronchial asthma may discover or rule out myocarditis before reporting negative result. It may occasionally account for sudden deaths.

L.J.H.

PROBLEMS IN THE DIAGNOSIS OF BRONCHIAL ASTHMA

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THE diagnosis of bronchial asthma is not difficult. Yet even experienced allergists are confronted practically daily with certain diagnostic problems. Some of these problems have been thoroughly dealt with in the literature, whereas others have been neglected. On some, statistics are available, but the issues at hand are not as yet clear. These questions will be discussed as follows: (1) Certain features concerning the differential diagnosis; (2) some diseases occurring simultaneously with bronchial asthma; (3) the common complications; (4) some rare complications of allergic asthma which may or may not have an etiological relationship to this disease.

DIFFERENTIAL DIAGNOSIS

The fact that all lung diseases and some extrapulmonary thoracic conditions may be accompanied by wheezing and dyspnea and thus may camouflage the clinical picture of bronchial asthma, formerly has accounted for a great deal of confusion. Even now, we find occasional autopsy reports in which the distinction of true bronchial asthma from nonallergic wheezing has not been carried out. It is not necessary to dwell on this question here. However, a common fallacy to which the more experienced allergist is often subject should be emphasized. In our endeavor to make the correct diagnosis, we sometimes fail to realize that such disorders as cancer of the lungs, foreign body in the lungs, a syphilitic heart, pulmonary abscess—in other words, conditions which produce considerable wheezing—may occur simultaneously in patients with allergic asthma. Their presence does not justify neglect of the patient's allergic state.

Concerning the differential diagnosis, a few points should be brought out which are usually not sufficiently stressed in textbooks: If wheezing is localized in a certain pulmonary area instead of being equally distributed throughout the lungs, one should always consider the possibility of a non-allergic process. If râles are present in addition to asthmatic bruits, some disease other than allergic asthma or some of its complications should be suspected, usually pneumonitis or bronchiectasis. A simple sign, sometimes helpful in establishing the diagnosis, is the observation of the patient's position. When an "asthmatic" patient is lying down, he should be suspected of having some other disease. Some of us have utilized, as a diagnostic criterion, the patient's response to epinephrin. This cannot be accepted without reservation. Not all allergic asthmatic patients respond to epinephrin and, conversely, patients with nonallergic wheezing obtain relief from it occasionally. When allergic asthma is complicated by pneumo-

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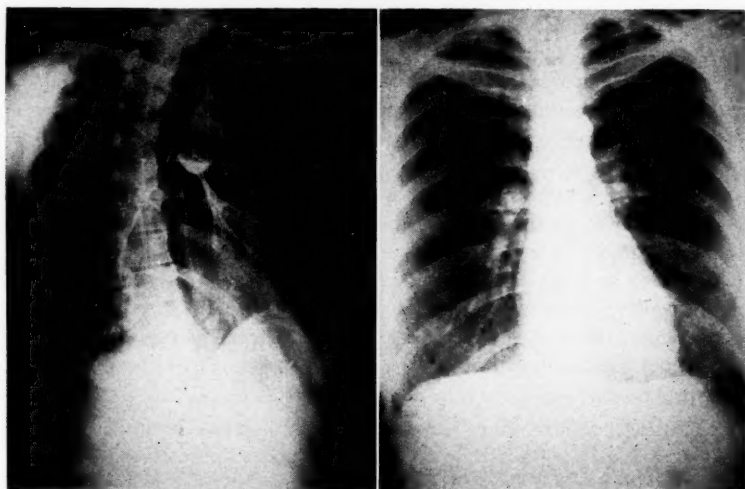


Fig. 1. (left) Case 1. Miss J. B., thirty-four years old. Partial obstruction of main bronchus in pulmonary tuberculosis simulating asthma. Note distention above the constricted area, visible after lipoidal injection.

Fig. 2. (right) Case 2. Mrs. B. L., thirty years old. Small area of active tuberculosis in left apex of two weeks' duration in an allergic asthmatic patient.

nit, epinephrin is of little value. When there is doubt concerning the diagnosis, a most reliable feature in the patient's history is the question of whether or not nasal symptoms have been present before, or are associated with, the asthmatic condition. If we fail to obtain this history, we should be skeptical about making the diagnosis of allergic asthma.

COINCIDENCE OF ASTHMA WITH OTHER DISEASE

It is assumed today that the allergic wheal is liable to occur in practically any part of the system. Therefore, any ailment occurring simultaneously with asthma should be scrutinized as being etiologically related to it. There are two diseases which have been said to occur very rarely in association with bronchial asthma; namely, diabetes and tuberculosis. Thyroid diseases and heart disturbances, on the other hand, have been identified as occurring more frequently in the asthmatic than in the average individual.

The question of diabetes (Beckman¹) can be easily disposed of, as all of us have not only seen this combination, but are quite familiar with the occurrence of sensitivity to insulin, which so often aggravates existing allergic asthma. I had occasion to observe the reverse relationship—namely, that an asthmatic state lowered the sugar tolerance.

The question of tuberculosis is more complex. Some German clinicians stated that these two diseases could not occur simultaneously, while others held that asthma originated from tuberculosis. The literature has been well

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summarized recently by Tooker and Davidson.⁵ Through co-operation with several tuberculosis specialists in Detroit, I have had an opportunity to observe a rather large group of cases presenting the combination of tuberculosis and asthma. This experience has brought out the following facts:

1. Asthmatic wheezing is encountered during the course of tuberculosis and is easily confused with asthma. Enlarged tubercular glands, strictures of bronchi, mucus and caseous material lodged in the bronchial tubes may induce bronchospasm and considerable wheezing in patients who are not allergic. Figure 1 (Case 1, Miss J.B., thirty-four years old) illustrates a bronchial stricture of tuberculous origin. Wheezing remained the most conspicuous manifestation at a time when the healing of the tuberculosis had progressed very satisfactorily.

2. Allergic asthma may become complicated by tuberculosis. This has been rare among my patients. That it does occur is illustrated by Case 2 (Mrs. B. L., thirty years of age) a patient with allergic asthma, who developed what appeared to be an upper respiratory infection with temperatures ranging up to 101 degrees. When she failed to improve promptly, the x-ray (Fig. 2) revealed a very small acute tubercular focus. This was associated with positive sputum.

3. Tuberculosis may be followed by allergic asthma. This, as well as hay fever, in the tuberculous patient is not uncommon. In treating these patients with pollen extracts, generalized reactions should be carefully avoided as they may induce the flare-up of the tuberculous lesions.

4. In three asthmatic patients with healed tuberculosis, I have observed strong skin reactions to tuberculin while the usual skin tests for allergy were not conclusive. Although there was a typical background of allergy, they had not responded to the usual allergic management. Upon instituting tuberculin treatment (Van Leeuwen⁸) with very small doses, these patients were completely relieved of asthma. They may have been primarily sensitive to tuberculin.

There is a strong feeling among some clinicians that hyperthyroidism plays a part in the asthmatic state. This is evidenced by the frequency with which these patients are subjected to metabolic studies. Indeed, the fast pulse, so commonly encountered during asthmatic attacks, the existing emaciation, often accounted for by sudden loss of fluid, may lead to this belief. Others have associated a low metabolic rate with asthma. Systematic metabolism studies on a large group of asthmatic patients have been carried out by some, but never published, evidently because they yielded no deviation from the normal state. On several occasions I encountered asthmatic persons whose disease responded very promptly to thyroid medication and others to the removal of a hyperplastic thyroid. Such an instance is Case 3 (Mr. J. S., fifty-three years of age), who had been in an extreme, chronic, asthmatic state. He was sensitive to many antigens. He

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had taken large doses of epinephrin. His asthma failed to improve from allergic management, but cleared up promptly upon thyroidectomy.

There has been some controversy as to whether or not an asthmatic patient is more likely to develop a heart disease than a normal individual. Two symptoms which are very pronounced in practically every asthmatic person have led to speculation on this possibility—namely, the occurrence of dyspnea upon the slightest exertion, and the presence of a fast pulse. In interpreting some of the statistical material available, which is summarized by Urbach⁷, we should be aware of the following facts: Heart disease is a very common disease. If present in an asthmatic person, the enlarged heart may, through pressure on the air passages, contribute to the asthmatic wheezing. This effect may be enhanced by existing pulmonary congestion from cardiac decompensation. Moreover, the continued use of such drugs as ephedrin and epinephrin in asthma may lead to cardiac damage. That allergic asthma will lead to significant changes in the heart, is unlikely for the following reasons: (1) In the average asthmatic person such manifestations as nycturia, edema, enlargement of the liver, are rare. (2) The typical x-ray study of a patient with asthma, even though it be of years' standing, does not show an enlargement of the heart. (3) The electrocardiographic changes noted in asthmatic persons (Harkavy and Romanoff⁸) are not impressive and may disappear after the subsidence of the attack. This is in line with the cardiac findings at autopsy in asthmatics (Lamson et al.⁴) which occasionally reveal acute dilation of the right heart, but no changes indicative of *chronic* disease.

COMMON COMPLICATIONS OF ASTHMA

The three common complications of allergic asthma are sinus disease, pneumonitis, and bronchiectasis. A proper evaluation of the condition of the sinuses, as well as of the tonsils, in allergic diseases is of great importance because of its therapeutic aspect. Enlarged tonsils, waterlogged nasal membranes, septum deviation, enlarged turbinates, and cloudy sinuses are generally accepted as resulting from the asthmatic state rather than causing it. Nevertheless, much remains to be clarified as to whether these structures should be treated surgically. Our greatest fallacy, I believe, is the undue stress of, and reliance on, such features as the presence or absence of eosinophil cells in the nasal mucus, the occasional findings of pus and cloudiness on transillumination or on x-ray evidence in the sinuses. There are two indications for a nasal operation in asthma: (1) chronic suppurations and chronic empyema of the sinuses; (2) continued interference with ventilation of the nose and drainage of the sinuses. In either case emphasis should be placed on chronicity and on the fact that a previous attempt at allergic management has failed to bring about a noticeable improvement. Also, concerning the indication for tonsillectomy in asthmatic persons, further clarification is needed. It has been demonstrated repeatedly that tonsillectomy may be followed by con-

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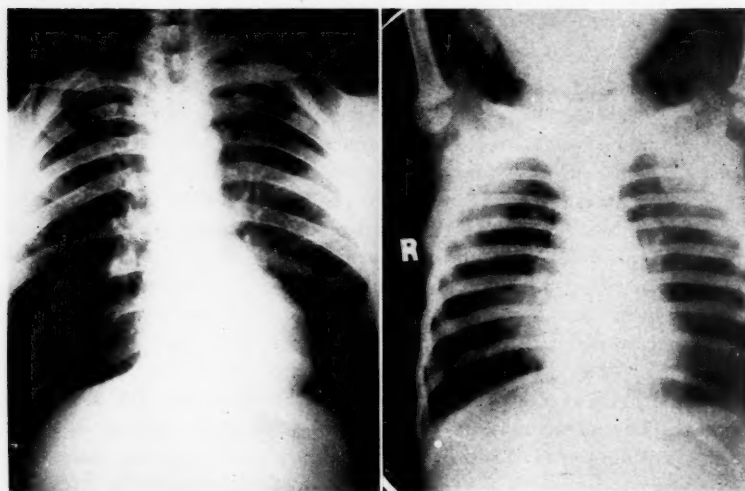


Fig. 3 (left) Case 4. Mr. V. B., thirty-five years old. Low-grade pneumonia, probably from allergic pulmonary edema, occurring suddenly through inhalation of pigeon feathers.

Fig. 4. (right) Case 5. B. W., two years old. Pneumonitis (chronic) in right lower lung, resulting from obstruction of a bronchus by mucus.

siderable aggravation of the asthmatic state. According to our own statistical studies¹⁰, not only the asthma fails to be relieved, but also other conditions for which the operation is performed, such as arthritis and ear infections, improve less readily than in nonallergic individuals. In other words, what appears to be infected tonsils and cervical glands, may actually represent waterlogged, edematous, hyperplastic lymphoid tissue superseded by secondary infection, changes corresponding to the condition of the mucous membranes of sinuses and bronchi. However, we should not accept these facts dogmatically. I observed several patients with enlarged tonsils whose asthma was refractory to any treatment until the tonsils were removed. It has been my practice to advise tonsillectomy, if there is a history of *frequent* febrile tonsillitis and if the clinical course of asthma indicates that we are dealing with an infectious type of asthma rather than with primary sensitivity to the common antigens. The morphological appearance of the tonsils or adenoids matters little in the indication for the operation.

During the course of allergic asthma, various types of pneumonitis are encountered, the proper clinical evaluation of which may present great difficulties.

1. There is the usual infectious type of pneumonia brought on by the common organisms of the disease. Whether or not its course is more violent and fulminating than that in a normal individual is difficult to state.
2. In asthma of short duration, especially in infants and young children,

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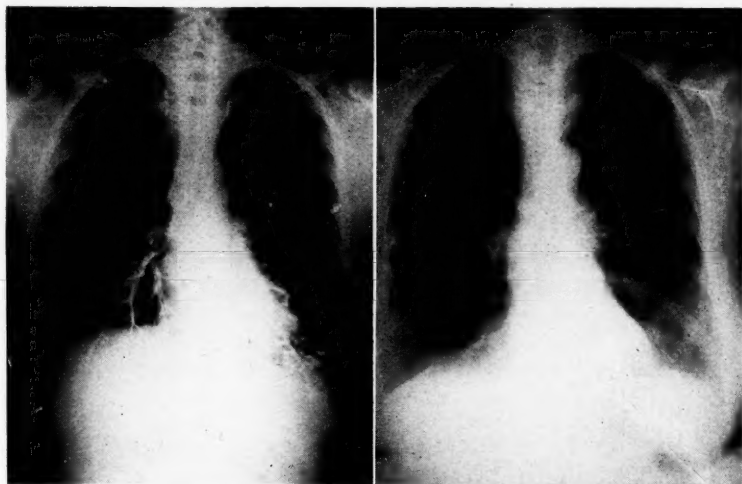


Fig. 5. (left) Case 6. Mr. A. S., thirty-four years old. Extensive saccular bronchiectasis confined to left lower lobe in a hay-fever patient, probably a congenital process causing no symptoms other than some cough in the morning.

Fig. 6. (right) Case 7. Mrs. H. W. H., seventy-five years old. Atelectasis of right lower lobe in an allergic asthmatic.

a certain type of pneumonitis occurs which can be regarded as a part of the clinical picture of the asthmatic attack (Waldcott⁹). This is the "pneumonia" which the patients relate in their history as having brought on the first attack of asthma. It is an allergic edema which becomes infiltrated with leukocytes after several hours. It is best illustrated by Case 4 (Mr. V. B., thirty-five years of age), who had always been in perfect health. On entering a pigeon coop he suddenly developed a cough, wheezing, and pronounced shock (Fig. 3). This was followed, after six hours, by moderate temperature lasting for three days. This episode was the beginning of a long course of asthma, primarily due to pigeon feathers. In another case, described elsewhere in detail⁹, a child developed shock and fever shortly after ingestion of milk. The pathological section from the lungs of this patient illustrates how small areas of edema become infiltrated with leukocytes at their periphery.

3. Some assume that atelectasis resulting from obstruction of small bronchi with mucus might account for secondary pneumonitis, the obstructed areas becoming subsequently infected. This mode of pneumonitis is demonstrated in the x-ray (Fig. 4) of a two-year-old girl (Case 5, B.W.) with allergic asthma. A mucous plug obstructed a large bronchus, accounting for fever and consolidation in this area for several months. This condition cleared up promptly upon removal of the mucus bronchoscopically and upon dilatation of the resulting scar in the bronchus. While the involvement of such a large pulmonary area as in this case is relatively

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rare, smaller lesions from obstructed secondary bronchi are frequently encountered during asthmatic attacks.

4. Through the investigation of Harkavy² and others, the so-called "Loeffler's syndrome" has been given general attention, a pneumonialike infiltration characterized by fever, high leukocytosis, and high eosinophilia. The lesions are transient, occurring in various parts of the lungs at different times. It is thought that this condition may originate from allergic reactions in capillary vessels in the lungs.

We need not dwell at length on bronchiectasis. There are two types, the cylindrical and the saccular. The latter type is rare and, as in Case 6 (Mr. A. S., thirty-four years of age), might represent a coincidence with asthma (Fig. 5). Even extensive bronchiectasis is not always as hopeless as it appears to be. I have seen many such patients improve considerably from allergic management in conjunction with bronchoscopic lavages. It is likely that small bronchi, which are greatly dilated and have been filled with mucus and pus during the course of a long-standing attack, can regain their normal elastic state after the pus has been removed and is prevented from reappearing.

RARE COMPLICATIONS OF ASTHMA

The following three cases are, I believe, rare complications of bronchial asthma—namely, atelectasis of a whole pulmonary lobe, cystic degeneration of the lungs, and multiple, spontaneous fractures of the ribs. It is possible that these manifestations may be coincidental. Others (Tuft⁶)* have encountered massive atelectasis as sequelae of asthma.

Atelectasis of Pulmonary Lobe.—Mrs. H. W. H., aged seventy-five (Case 7), had had allergic asthma since the age of seventeen. The attacks were usually preceded by allergic rhinorrhea and by upper respiratory infection. There was no tendency to seasonal aggravation.

About two months ago a severe asthmatic attack occurred during which she became pulseless and extremely short of breath requiring constant attention by her physician for five hours (heart stimulants, oxygen, and aminophyllin). Since then, the dyspnea and extreme cyanosis were present continuously.

Examination showed a well-developed, well-nourished female with marked dyspnea and cyanosis. There was physical evidence of marked asthma; there was x-ray evidence (Fig. 6) of complete atelectasis of the right lower lobe of the lung. In addition there was tortuosity of the aortic knob, pleural thickening over the apices, and a few calcified nodes in the hilus and in the parenchyma of the right lung. Particular attention was paid to ruling out a neoplasm and a heart disease by subsequent x-ray examinations. After one month the persistence of the atelectatic lobe was still evident, but another check, two years later, showed normal lungs.

*Spontaneous rib fractures were reported to me orally by several clinicians viewing my AMA exhibit, 1940.

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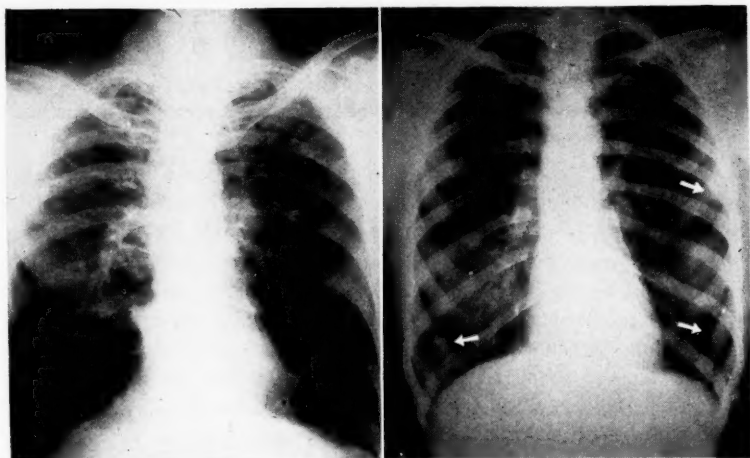


Fig. 7. (left) Case 8. Mr. L. A., fifty-three years old. Cystic degeneration of lungs (ruptured alveoli) in a chronic asthmatic patient. Ten years previously the patient had a left-sided spontaneous pneumothorax. Note air blebs especially in lower portions of lungs.

Fig. 8. (right) Case 9. Mrs. E. C., thirty years old. Spontaneous rib fractures in a case of chronic allergic asthma.

The asthma responded very well to allergic management. The patient refused bronchoscopic aspiration which was indicated. Atelectasis of a whole lobe may well be brought about by obstruction of the main bronchus.

Cystic Degeneration of Lungs.—Mr. L. A., fifty-three years old (Case 8), had had allergic asthma since the age of twelve. Up to 1925 the attacks had occurred intermittently, mostly in summer and fall. During later years they were continuous. In May, 1932, the patient experienced a sudden collapse and severe pain in the left side radiating into the apices. At that time the x-ray revealed advanced emphysema and a left-sided pneumothorax. Complete intradermal skin tests had shown positive reactions to a large group of antigens, especially to ragweed and house dust.

On examination, in 1941, the patient showed extreme emaciation with great respiratory distress. The chest was barrel shaped. There was little expansion. Wheezing and coarse râles were heard throughout the lungs. Heart sounds were distant. X-ray examination (Fig. 7) showed extensive bilateral emphysematous changes with multiple large emphysematous bullae.

It may be assumed that during the years of severe cough and dyspnea, the patient "blew out" an emphysematous area near the periphery of the left lung, first causing a pneumothorax and later a cystic degeneration of the lungs. Both pneumothorax and ruptured alveoli have been seen in other patients with allergic asthma.

DIAGNOSIS OF BRONCHIAL ASTHMA—WALDBOTT

Multiple Fracture of Ribs. Mrs. E. C., thirty years old (Case 9), had had asthma since the age of nine. The asthma was originally precipitated by ragweed hay fever. Four months before I saw her, the patient experienced severe coughing spells during which extreme pains in various parts of the ribs were noted.

The physical examination revealed nothing significant other than considerable emaciation (90.5 pounds) and typical asthma throughout both lungs, cloudy sinuses and evidence of fractured ribs.

The x-ray examination showed four rib fractures in different stages of healing. Blood studies and bone marrow puncture were performed to rule out certain hematological diseases and metastatic tumors. They were negative except for a 10 per cent blood eosinophilia. Calcium and phosphorus levels of the blood were normal.

The spontaneous rib fractures were probably due to intense coughing during an attack.

SUMMARY

1. Various features in the differential diagnosis of bronchial asthma are emphasized.
2. The association of asthma with other allergic and nonallergic conditions is reviewed.
3. Common and some rare complications of asthma are related.

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SUCCESSFUL TREATMENT OF EXTREME ALLERGY TO BEE BODY AND BEE VENOM. McLane, E. G., *Minnesota Med.*, 26:1061, (Dec.) 1943.

McLane reports a case in which marked sensitivity to bee body and bee venom was overcome by graduated injections of whole bee extract, followed by carefully spaced bee stings. Inasmuch as this extract protected the patient from both bee emanations and stings, the author suggests that there is a common substance present in both allergic sources. Bibliography.

W.J.H.

UNUSUAL COMPLICATIONS OF BRONCHIAL ASTHMA: AIR IN EXTRA-PULMONARY SPACES

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THERE are few acute clinical manifestations which are more distressing and dramatic to the physician and patient alike than the asthmatic paroxysm to which is added the consequences of pulmonary rupture. The course taken by the liberated air determines whether there will be subcutaneous emphysema, spontaneous pneumothorax, mediastinal emphysema, or a combination of any of these. Blood vessels, fibrous tissue and old adhesions are among the factors which direct the escaped air. Over the past year we have seen a number of asthmatic patients who suffered such complications. From this series we have selected instances which represent the typical course of events.

SPONTANEOUS PNEUMOTHORAX

Although pneumothorax is generally considered to be a complication of pulmonary tuberculosis, it is the opinion of phthisiologists¹¹ of wide experience that tuberculosis is the etiologic agent in not over 10 per cent of the cases. In view of the marked thinning of the alveolar walls and increase in intra-alveolar pressure so often present in chronic asthma, it might be assumed that spontaneous pneumothorax will occur frequently in this condition. In a survey of the literature in this regard, we² find only about twenty-one such instances.

Detailed discussion of these serves little useful purpose because of their great similarity. One of our patients was a forty-eight-year-old white man who was suddenly seized with an attack of severe dyspnea and orthopnea. In addition to the presence of sibilant râles, findings on physical examination indicated displacement of the heart and trachea to the left. The patient died on the fourth hospital day, and autopsy revealed collapsed blebs at the apex of the right lung in addition to the pneumothorax.

Classically, in these patients, the findings differ little from those seen in uncomplicated pneumothorax except that, if the complication occurs during the asthmatic seizure, the characteristic signs of bronchial asthma are superimposed. Among the outstanding symptoms are pain, dyspnea, cough and collapse. Typically, on physical examination, there is a decrease in fremitus, breath and voice sounds. As in the reported instance hyperresonance to percussion can be demonstrated together with dis-

¹From the departments of Medicine and of Preventive Medicine, Tulane University School of Medicine, and from the Charity Hospital of Louisiana, New Orleans, La.
²Presented at the First Annual Meeting of the American College of Allergists, Chicago, Illinois, June 10 and 11, 1944.

placement of the heart and mediastinal structures to the unaffected side. Roentgen examination confirms the physical findings and in many instances reveals small degrees of pneumothorax which would otherwise be overlooked.

MEDIASTINAL EMPHYSEMA AND SUBCUTANEOUS EMPHYSEMA

Although mediastinal emphysema was first described by Mueller in 1888⁸, it received little notice until 1937 when Hamman⁴ directed attention to it.

Because individuals having chronic asthma are frequently in the age group liable to have coronary artery disease, a particularly perplexing differential diagnostic problem may arise when this condition occurs with asthma. Indeed, in Hamman's first case the patient, a physician, was thought to have myocardial infarction; only later, when air was discovered in the anterior mediastinum, was the correct diagnosis established.

One of our patients was seen in the admitting room of Charity Hospital with the chief complaints of asthma and substernal pain. On examination the findings, which are now recognized as classical of mediastinal emphysema, were elicited. Later, in the ward, swellings in either side of the neck were detected. Examination revealed the pathognomonic crepitations of air in the subcutaneous tissues. The outstanding finding of mediastinal emphysema is a peculiar loud, crackling, bubbling sound which is synchronous with the heart beat. As Hamman and others have observed, we too on occasion have been able to hear this crunching noise at some distance from the patient without the aid of the stethoscope. Although it has been emphasized that this condition may occur without the least effort and regardless of the position of the patient, it will readily be appreciated that severe respiratory muscular imbalance will precipitate the syndrome.

The entrance of air into the mediastinum with forceful separation of those structures results in substernal pain not unlike that found in myocardial infarction. It is well known that severe pain is not a part of the asthmatic picture, and its presence therefore should immediately direct the attention of the attending physician to some complication. As Hamman⁴ has pointed out, there are negative points of great value in making the diagnosis. These are an absence of constitutional symptoms and of evidence of shock, a normal temperature, and lack of change in blood pressure and leukocyte count. On physical examination, the area of cardiac dullness may be replaced by one of resonance to hyperresonance.

It is well to emphasize that even in the absence of the typical physical findings the presence of air in the mediastinum can be demonstrated roentgenologically. In the above case the pneumothorax which was present was small and could be detected only by roentgen-ray study.

The air which has accumulated in the intrapleural space works its way, as Macklin⁷ has shown, along the sheaths of the blood vessels and the fascial planes until it reaches the hilus and in this manner finds its way into the anterior mediastinum where it is later absorbed. This is the usual sequence of events, however, as in our case, the air may subsequently work its way along fascial planes following the course of blood vessels and make itself known as subcutaneous emphysema about the base of the neck.

Subcutaneous emphysema is a rare complication of bronchial asthma as shown by the fact that a late review of the subject⁹ brought to light only eighteen cases from the world literature. Clinically, subcutaneous emphysema may involve not only the neck but may extend to the face, upper extremities, thorax, and abdomen, but only rarely does it involve the thighs. From the reported cases, it would appear that subcutaneous emphysema carries a good prognosis. To our knowledge, no deaths have been reported, and there have been no recurrences in spite of the fact that patients were subjected to further attacks of bronchial asthma. The condition is self-limited, and in from four days to two weeks recovery is usually complete. Most of the patients were young and distributed equally between the sexes.

DISCUSSION

Although emphysema is one of the most common complications of bronchial asthma, it is indeed interesting to note that pneumothorax occurs very rarely. It would appear that the thin avascular alveolar wall would be a perfect site for a laceration of lung tissue.

It might be well to point out that tension sufficient to produce rupture of the normal pleura does not result from even the most severe paroxysms of coughing, unless there is some anatomic or pathologic alteration, either congenital or acquired. West¹⁰ showed half a century ago that the normal pleura cannot be ruptured unless the intrapulmonary pressure exceeds 200 millimeters of mercury. It is paradoxical that rupture does not occur more frequently in emphysema, for Zahn¹² has shown that normally the alveolar wall plus the visceral pleura measures 0.13 to 0.24 mm., whereas in emphysematous lungs the thickness may diminish to as little as 0.03 mm.

The explanation of Castex and Mazzei¹, that in emphysema a progressive decrease in the negativity of the intrapleural pressure occurs so that finally this pressure approaches positive, and in this manner an equilibrium is established between the intrapleural and intra-alveolar pressures, is in our opinion the most logical explanation for the rarity of rupture of the blebs which occur so uniformly.

There are forces at work, however, which tend to disturb this attempt of the body to maintain homeostasis. We feel that regardless of the

cause, be it tuberculosis, congenital cyst, or an emphysematous valve vesicle, the rupture occurs through the intermediary of a valve vesicle. As Kjaergaard⁶ and Hyoshi⁷ have shown by postmortem studies, this

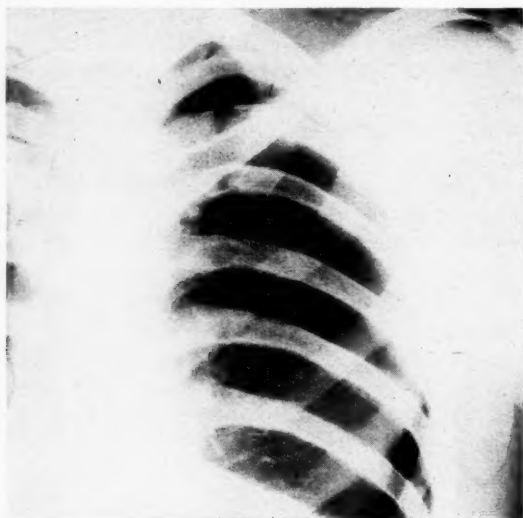


Fig. 1. Enlarged roentgenogram demonstrating the valve vesicle and partial pneumothorax.

valve vesicle actually occurs, and with each inspiration more air enters the vesicle than leaves it. In this manner, a sequence of events is established which allows for stretching and finally rupture of the vesicle. In Figure 1 (courtesy of Dr. J. L. Wilson), such a vesicle may be seen.

It has been pointed out elsewhere that there is greater danger of rupture on deep inspiration than following a paroxysm of coughing. In coughing, the tendency is for closer approximation of the lung to the chest wall. This results in a lessening of the positive pressure in the alveoli and a decrease of the negative pressure in the intrapleural space. Following a deep inspiration there is atmospheric pressure in the alveoli and a decrease of the negative pressure in the intrapleural space. Following a deep inspiration there is atmospheric pressure in the alveoli and negative pressure without, favoring rupture. We believe that the reason why spontaneous pneumothorax is not more frequent in bronchial asthma is that the expiratory element is definitely prolonged at the expense of inspiration.

It is well to point out, however, that in the pneumothorax which followed mediastinal emphysema, Macklin was unable to demonstrate a tear in the visceral pleura, but could show a definite tear in the mediastinal wall. As Hamman has shown, we must at least entertain the possibility

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that the initiating lesion for the pneumothorax may be the escape of air into the pleura from the mediastinum. There are reports of cases of this nature showing a fine sharp line running parallel to the border of the

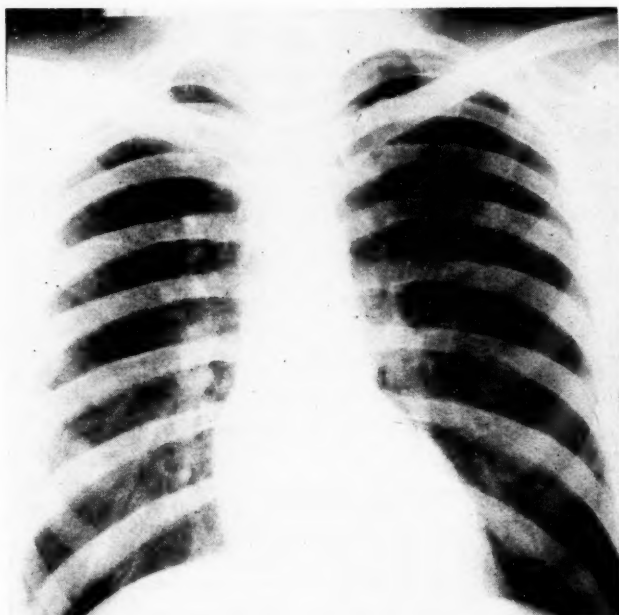


Fig. 2. Note fine sharp line running parallel to left border of heart.

heart on roentgen examination. We have had occasion to observe a similar instance, the roentgenogram of which is shown in Figure 2.

The outlook for patients with these complications of bronchial asthma is extremely good indeed. There is little doubt in our minds but that all these conditions, especially pneumothorax, occur much more frequently than is suggested by the literature.

As we have mentioned elsewhere, the physician should exercise restraint in the use of mechanical measures because the nature of the lesion is such that with little or no treatment the great majority of the patients completely recover. We should like especially to emphasize the dangers associated with tap of the pleural space and removal of the escaped air. This practice disturbs a protective mechanism—namely, the equality of pressure on either side of the alveolus. This pressure equality allows for a minimum of movement and maximum healing. Removal of air, then, sets into motion forces which lead to bronchopleural fistula and which may not only result in a tension pneumothorax but in a contaminated pleural cavity as well.

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We feel that bed rest for about a month and sedatives as needed are the most important points in the treatment, and that thoracentesis should be reserved for those cases of tension pneumothorax where the intrapleural pressure is such as to embarrass seriously the patient's respiration.

Once healing has been accomplished, the nitrogen factor of the escaped air, which is still in the pleural spaces, may be absorbed more rapidly by the use of oxygen in a concentration approaching one hundred per cent. Fine³ and his group, using this method, have been able to increase the diffusion pressure of the nitrogen between the pleural space and the blood vessels and in this manner bring about a more rapid absorption of this gas.

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PERIARTERITIS NODOSA; REPORT OF CASE. Lichtman, A. L., Stickney, J. M., and Kernohan, J. W.: *Proc. Staff Meetings of Mayo Clinic*, 18:500, (Dec. 15) 1943.

An illustrative case report. Histogenically, in periarthritis nodosa, there is necrosis of media with resulting extension of inflammatory reaction and repair into perivascular tissues. The subsequent infarction produces disability. Marked variation of vascular involvement is outstanding characteristic. Occlusion of vasa nervosum has been a constant observation of authors. Eosinophile cells are usually present in the inflammatory reaction. The symptoms vary with the degree of involvement of different organs and tissues, depending on the interruption of the blood supply. Asthma (in 15 to 20 per cent) eosinophilia (often 70 to 80 per cent), and peripheral nerve involvement are common characteristics of periarthritis nodosa. The etiology is probably allergic or infectious with neither definitely proven.

L. J. H.

POLLINOSIS IN SAN DIEGO COUNTY, CALIFORNIA
With a Proposed Method for the Estimation of the
Relative Importance of the Plants Concerned

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MOUNTAINOUS areas such as Southern California present a great diversity of topography and vegetation. To a large extent, the centers of habitation are surrounded by mountain ridges which act as more or less effective barriers to air-borne pollens so that each community is a problem in itself. The multiplicity of potential causes of pollinosis in such an area renders it necessary to determine as accurately as may be the significance of each of the plant species found.

Numerous authors have reported pollen counts and botanic surveys for various communities throughout the world. A review of the available literature revealed the astonishing fact that in none of these was all the necessary data given to evaluate quantitatively the actual or relative importance of the individual plant specimen involved, nor was any method or formula suggested for arriving at a quantitative expression for the over-all importance of each species after consideration of the various factors involved.

In rare instances in which the pollen of the individual species can be identified microscopically, pollen counts at suitable stations are adequate, but for all others field studies are necessary. It would seem indisputable that the importance in pollinosis of a given pollen species with respect to a given patient would be mathematically the product of the degree of the patient's sensitivity to that pollen and the amount of it to which he is exposed. It would also seem self-evident that the amount of pollen to which the patient is exposed can be expressed as the mathematical product of the abundance of the species, the amount of pollen produced in a given time per unit area, the period of pollination, and some factor which expresses the ability of the pollen to travel from the plant to the patient. Any quantitative evaluation must necessarily be an approximation since there are many variable factors such as the proximity of the plants to centers of habitation, the prevailing direction and velocity of the wind, the height from which the pollen takes off in its travel through the air, the existence of spicules or wings on the pollen, and, of course, the changing location of the patient himself. The toxicity of the pollen species varies with each patient but is determined roughly by skin testing.

The existence of these variable factors does not excuse us from trying to be as accurate as possible. It seemed desirable, therefore, to adopt some scheme which would bring into their proper relationship all of the factors which are susceptible of quantitative evaluation.

From the Rees-Stealy Clinic, San Diego, California.
Presented at the First Annual Meeting of the American College of Allergists, Chicago, Illinois, June 10 and 11, 1944.

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To this end we deliberately assumed as a standard, a hypothetical plant with a pollinating period of two months, a pollen diameter of 25 microns, a pollen production of 100, and an abundance of 10 on a scale of 1 to 10. To this hypothetical plant we assigned an importance rating of 100. It was assumed that the buoyancy of a pollen of a given size would be inversely proportional to the velocity of its fall in air. The velocity of fall in air at 20° C. for pollen of various sizes is given by Dahl and Ellis^{2,3} who based their calculations on Stokes' formula.[†] Hence the buoyancy factor may be determined by dividing the velocity of fall of a pollen of 25 microns diameter by the velocity of fall of the pollen in question. The pollen production of *Franseria acanthicarpa* (false ragweed) was assigned a rating of 100 because this species, among the plants in our locality, most closely resembles *Ambrosia elatior* (dwarf ragweed) which has been assigned a value of 100 by several other authors. Barrett,¹ in Salt Lake City, found it to have a pollen production value in that area of 65 as compared to 100 for *Ambrosia elatior*. The actual pollen production of *Franseria acanthicarpa* was found to be 1.7 gm. per day for one square meter of a pure stand when collected at the peak of pollination.

The importance rating of any given species may be determined with respect to this hypothetical plant by the following formula:

$$\frac{n}{2} \cdot b \cdot p \cdot \frac{a}{10} = \text{I.R.}$$

where

- n = number of months of pollination
- b = buoyancy factor
= $\frac{\text{velocity of fall of a pollen of } 25\mu \text{ diameter}}{\text{velocity of fall of the pollen in question}}$
- p = pollen production (*Franseria acanthicarpa* = 100 = 1.7 gm./day/sq. meter)
- a = abundance (scale of 1 to 10)
- I.R. = importance rating

*The following is taken from the tables of Dahl and Ellis²:

Diameter of pollen grains in microns	Velocity of fall (feet per second)
15	.022
18	.032
22	.048
25	.062
28	.078
32	.102
36	.129
40	.159
44	.192
48	.229
50	.248

*Example: *Lolium multiflorum* (Italian ray grass) (See Table IV, p. 36)

$$n = 5; b = \frac{.062}{.129}; p = 105; a = 4$$

$$\frac{5}{2} \times \frac{.062}{.129} \times 105 \times \frac{4}{10} = 52$$

†Stokes' formula: $V = \frac{2gr^2(d_1-d_2)}{9K}$

where

- V = velocity in cm./sec.
- g = acceleration of gravity = 980 cm. per sec.
- r = radius of the sphere
- d₁ = density of the sphere
- d₂ = density of the medium
- K = coefficient of viscosity of the medium (air at 20° C. to 23° C.) = 0.00018

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TABLE I. TOTAL POLLEN GRAINS FOUND ON ONE SQUARE INCH OF SLIDE
FOR ONE YEAR

	San Diego 1936-1941 (average)	Escondido 1936	Alpine 1936
Cupressus and Juniperus (cypress and juniper)	2921	1607	648
Gramineae (grass)	1320	1451	1342
Artemisia (sagebrush)	1073	2708	2094
Quercus (oak)	978	3104	40719
Chenopodiaceae and Amaranthaceae (goosefoot and pigweed)	456	414	1829
Ambroseae (ragweed)	452	404	1137
Adenostoma and Eucalyptus (chamise and eucalyptus)	371	499	566
Palmaceae (palm)	339	14	0
Schinus (pepper tree)	231	364	54
Olea (olive tree)	162	391	303
Other compositae (other than sagebrush and ragweed)	152	340	467
Platanus (sycamore)	51	89	50
Juglans (walnut)	39	205	37
Populus (cottonwood)	36	45	248
Alnus (alder)	35	20	185
Acacia (acacia tree)	35	48	4
Salix (willow)	14	222	240
Gramineae	1941		
Under 30 microns diameter	954		
31-40 microns diameter	672		
41-50 microns diameter	134		
over 50 microns diameter	27		

TABLE II. GRASS POLLENS GROUPED ACCORDING TO SIZE OF THEIR GRAINS

	Pollinating Period (months)	Importance	Pollen Size
Over 50 microns diameter			
Avena fatua (common wild oats)	2-4	10	53
41 to 50 microns diameter			
Spartina leiantha (cord grass)	6-9	4	47
Sorghum halepense (Johnson grass)	5-9	7	43
Bromus rigidus (broncho grass)	4-5	20	43
31 to 40 microns diameter			
Bromus carinatus (California brome grass)	2-4	3	39
Hordeum murinum (wall barley)	2-4	7	39
Bromus mollis (soft brome)	3-5	10	37
Lolium multiflorum (Italian ray grass)	3-7	50	36
Lolium perenne (English ray grass)	3-7	7	36
Distichlis stricta (salt grass)	5-7	5	32
Pestuca megalura (rattail fescue)	2-5	10	32
Under 31 microns diameter			
Polypogon monspiliensis (beard grass)	3-7	2	30
Cynodon Dactylon (Bermuda grass)	2-11	120	26
Poa annua (annual blue grass)	1-8	3	25

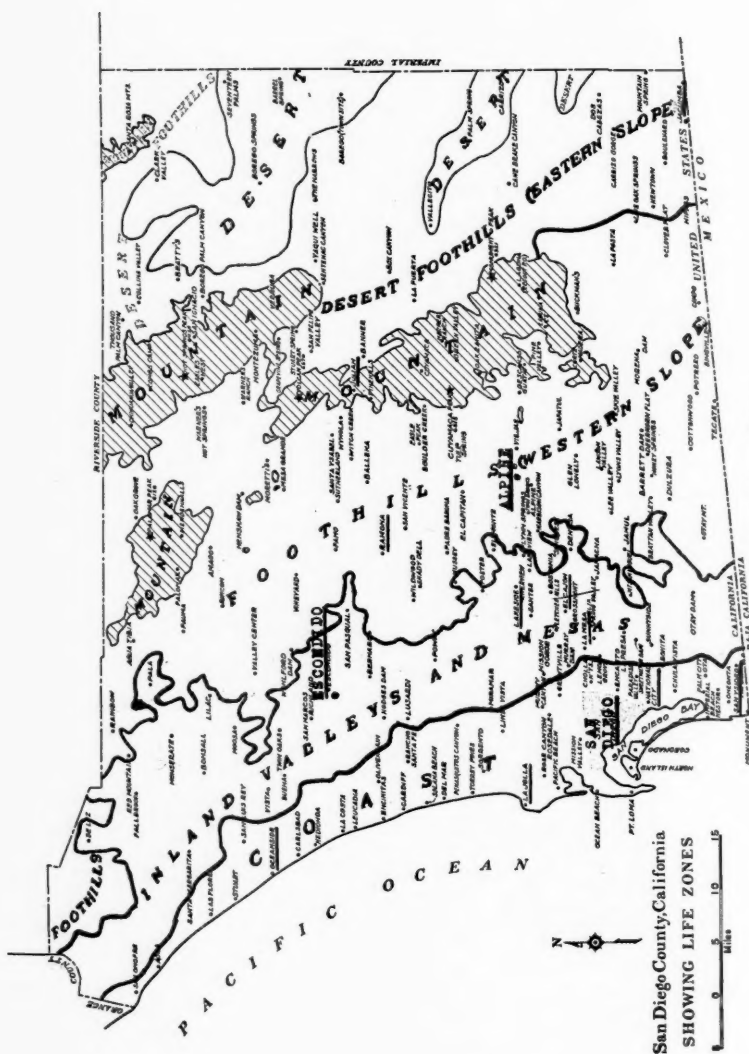


Fig. 1. Map of San Diego County

POLLINOSIS—HARSH ET AL.

POLLEN COUNTS — SAN DIEGO, CALIFORNIA — 1936

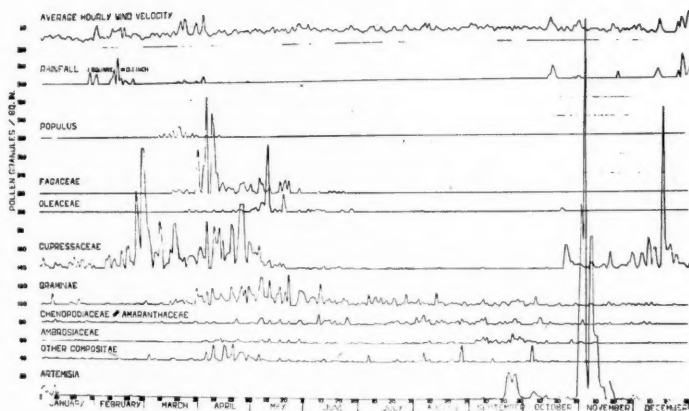


Chart I. Pollen Count for San Diego, California, 1936

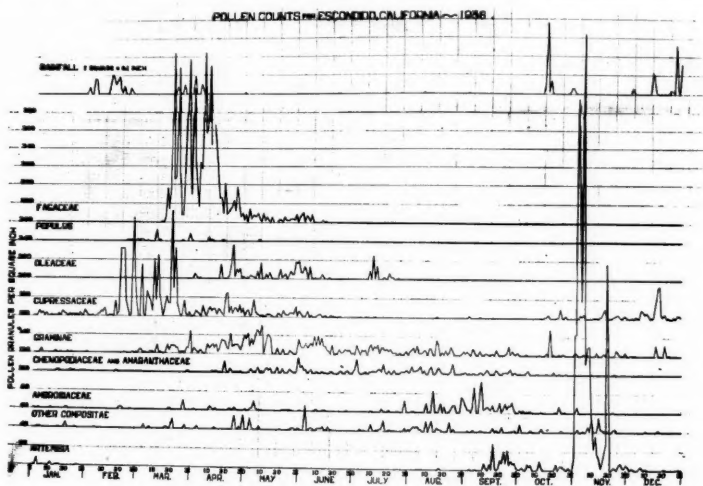


Chart II. Pollen Count for Escondido, California, 1936

It will be seen that the factors in the accompanying formula correspond to three of the five postulates enumerated by Thommen² which determine the importance of a given species in pollinosis. A fourth factor, toxicity, is left out of the equation inasmuch as it varies with each patient. The fifth factor, namely, that the species be wind pollinated, is not absolutely essential.

Data collected over a period of seven years in the study of the etiology

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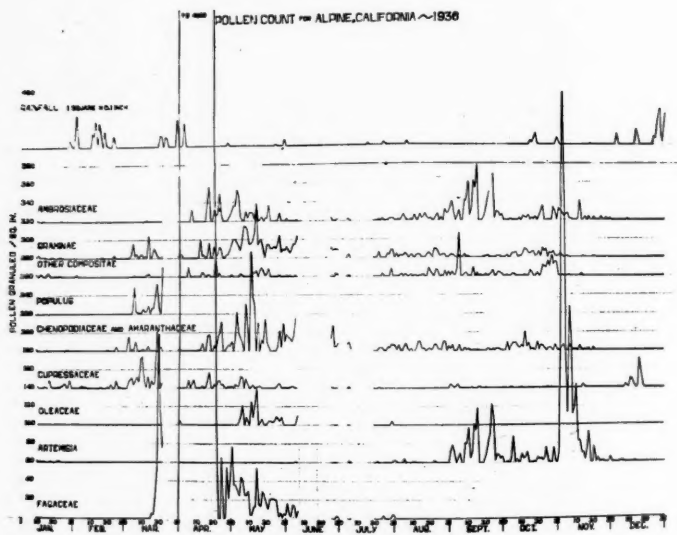


Chart III. Pollen Count for Alpine, California, 1936

of pollinosis in San Diego County, were subjected to evaluation by means of this formula.

PROCEDURE

San Diego County is approximately the size of the state of Connecticut. It is bounded on the west by the Pacific Ocean and on the east by the Colorado Desert. Its northern and southern boundaries pass through thinly populated areas. The Coast Range runs north and south through the center of the county and rises to as high as 6,500 feet. The prevailing winds are westerly so that in consequence the relative humidity is quite high along the coast and very low along the eastern border. Rainfall averages about ten inches at the coast, as high as 30 inches in the mountains, and about 2.5 inches at the eastern border. The rains occur almost exclusively in the winter months. Killing frosts are unknown in the coastal area but may occur in the mountains. The map indicates that the topography of San Diego County falls into six fairly distinct life zones, namely, the coast, the inland valleys and mesas, the western foothills of the Coast Range, the mountains, the eastern foothills, and the desert. The last three are sparsely populated.

In 1936, Stealy and McMichael¹² published the results of daily pollen counts at four representative stations within the city limits of San Diego. In this present study the observations at the central station in San Diego were continued as representative of the coastal life zone and in addition, observations were made at Escondido as representative of the inland valleys and mesas and at a resort thirty miles inland, at an elevation of 2,200

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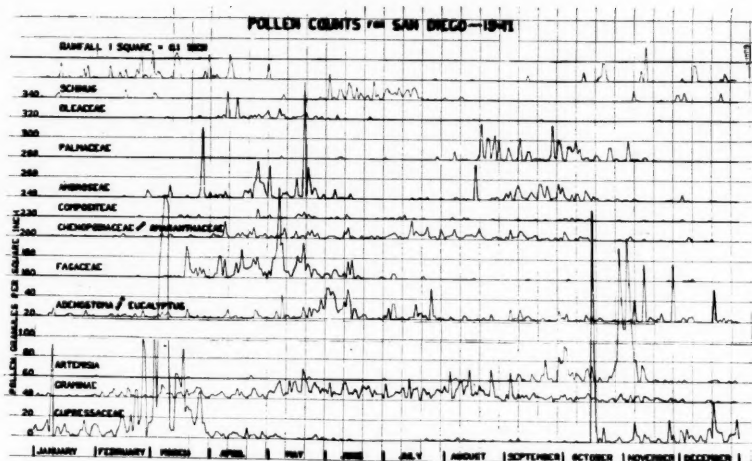


Chart IV. Pollen Count for San Diego, California, 1941

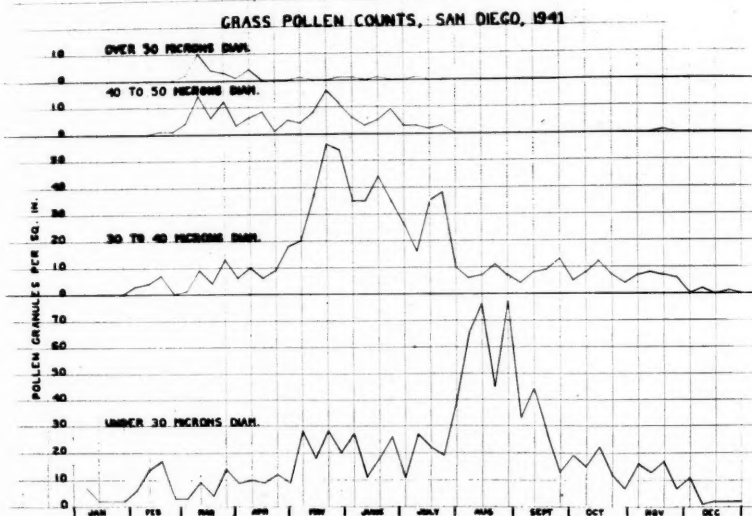


Chart V. Grass Pollen Counts, San Diego, California, 1941

feet, located two miles east of the village of Alpine, as typical of the western foothills region. Charts I, II, and III give the results of these pollen counts for the more important groups of pollens and Table I gives the sum of the daily pollen counts for one year of each pollen group identified. The values in the charts represent the pollen found on one square inch of slide after a twenty-four-hour exposure. The slides were exposed horizontally in a sheltered holder at the level of the roof of a two-story

TABLE III. HAY FEVER PLANTS OF SAN DIEGO COUNTY, CALIFORNIA
Relative Abundance—Scale 1-10

	Oceanside	La Jolla	W. San Diego	E. San Diego	Coronado	National City	San Ysidro	COAST	La Mesa	El Cajon	Lakeside	Escondido	Fallbrook	VALLEYS	Ramona	Alpine	Julian	Jacumba	MOUNTAINS	SAN DIEGO COUNTY
POLYGONACEAE (buckwheat family)																				
Rumex crispus (curly dock)	1	2	1-1	1	1-1	2	1	1	2	2	3	3	2	2	2	1	2	1	1	2
CHENOPODIACEAE (goosefoot family)																				
Chenopodium murale (nettle-leaf goosefoot)	3	2	2	2	3	5	3	3	3	1	1	1	2	2	1	1	1	1	1	3
Chenopodium album (lambs quarters)	1	1	1	1	1	1	1	1	1	3	4	3	3	3	1	1	1	1	1	3
Chenopodium ambrosioides (Mexican tea)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Atriplex canescens (sagebrush)	4	3	6	5	8	9	5	7	4	2	5	5	1	1	4	4	2	2	3	5
Atriplex Breweri (dense scale)	2	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Atriplex canescens (shad scale)	2	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Salicornia pacifica (pickleweed)	6	2	1	1	1	6	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Suaeda californica (sea blite)	2	2	2	2	1	4	4	3	1	1	3	1	1	1	1	2	3	3	2	2
Salsola kali, tenuifolia (Russian thistle)	1	2	2	2	1	1	3	2	1	1	1	1	1	1	1	1	1	1	1	1
AMARANTHACEAE (amaranth family)																				
Amaranthus retroflexus (rough pigweed)			1-1	1	1	4	2	2	2	1	1	6	4	3	1	1	1	1	1	2
PLATANACEAE (sycamore family)			1-1	1	1	1	1	1	1	1	1	1	2	1	1	2	1	1	1	1
Platanus racemosa (western sycamore)																				
LEGUMINOSAE (pea family)																				
Acacia (sps)(acacia)	3	3	2	4	2	3	1	3	4	3	1	2	2	2	2	2	1	1	1	2
ANACARDIACEAE (sumac family)																				
Schinus molle (pepper tree)	1	1	4	4	3	5	1	4	3	3	6	2	1	4	1	1	1	1	1	3
MYRTACEAE (myrtle family)																				
Eucalyptus (sps)	5	3	2	4	3	4	2	4	5	5	6	5	2	5	1	1	1	1	1	4
OLEACEAE (olive family)																				
Olea europaea (olive tree)	2	1	1	1	1	4	1	2	3	5	4	1	6	4	1	1	1	1	1	3
COMPOSITAE (composite family)																				
Hymenoclea monogyra (desert fragrance)																				
Ambrosia psilostachya (western ragweed)	4	3	3	5	1	2	2	4	7	7	8	8	7	2	6	5	5	4	5	2
Franseriaa cantharidifolia (false ragweed)	6	4	4	4	7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Xanthium bipinnatifidum (beach bur)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Xanthium pennsylvanicum (cocklebur)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Artemisia californica (coast sagebrush)	4	10	1	3	1	2	3	1	2	6	2	3	3	3	2	1	2	1	2	2
Artemisia tridentata (Indian hair tonic)			1-1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Artemisia Douglasiana (mugwort)																				

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TABLE III. HAY FEVER PLANTS OF SAN DIEGO COUNTY, CALIFORNIA
Relative Abundance—Scale 1-10

	Oceanside	La Jolla	W. San Diego	E. San Diego	Coronado	National City	San Ysidro	COAST	La Mesa	El Cajon	Lakeside	Escondido	Fallbrook	VALEYS	Ramona	Alpine	Julian	Jacumba	MOUNTAINS	SAN DIEGO COUNTY
PINACEAE (pine family)																				
Quercus agrifolia (black oak)																				
Juniperus californica (Calif. juniper)																				
GRAMINEAE (grass family)																				
Sorghum halepense (Johnson grass)																				
Echinochloa crus-galli (barnyard grass)																				
Phalaris minor (small canary grass)																				
Polypogon monspeliensis (beard grass)																				
Avena fatua (common wild oats)																				
Avena barba (Aleger wild oats)																				
Cynodon Dactylon (Bermuda grass)																				
Spartina lantha (cord grass)																				
Distichlis spicata, laxa (salt grass)																				
Poa annua (annual blue grass)																				
Festuca megalaria (rat tail fescue)																				
Bromus carinatus (Calif. brome grass)																				
Bromus mollis (soft brome grass)																				
Bromus rubens (red brome grass)																				
Bromus rigidus (broncho grass)																				
Lolium perenne (English ray grass)																				
Lolium multiflorum (Italian ray grass)																				
Hordeum murinum (wall barley)																				
SALICACEAE (willow family)																				
Populus Fremontii (Fremont cottonwood)																				
Salix lasiolepis (arroyo willow)																				
BETULACEAE (birch family)																				
Alnus rhombifolia (white alder)																				
FAGACEAE (beech family)																				
Quercus Kelloggii (Calif. black oak)																				
Quercus agrifolia (coast live oak)																				
Quercus engelmannii (mesquite oak)																				
Quercus dumetorum (scrub oak)																				
Quercus chrysolepis (maul oak)																				
URTICACEAE (nettle family)																				
Urtica gracilis, holoserica (creek nettle)																				

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TABLE IV. PERTINENT DATA ON PLANTS OF IMPORTANCE IN POLLINOSIS IN SAN DIEGO COUNTY, CALIFORNIA

	Pollinating period (in months of year)	Pollen size (in microns)	Pollen production at maximum intensity*	Percentage of patients reacting			Plant abundance (Scale 1-10)	Importance (disregarding toxicity)†
				1+	2-4	Total		
PINACEAE (pine family)								
Cupressus macrocarpa (Monterey cypress)	12- 5	25	400	10	3	13	3	300
Juniperus californica (California juniper)	11- 5	32	200	2	1	3	1	40
GRAMINEAE (grass family)								
Sorghum halepense (Johnson grass)	5- 9	43	20	20	12	32	2	7
Echinochloa crus-galli (barnyard grass)	7-10	33	7			20	1	2
Phalaris minor (small canary grass)	4- 6	39	35	18	16	34	1-	1
Polypogon monspiliensis (beard grass)	3- 7	30	7				2	2
Avena fatua (common wild oats)	2- 4	53	25	11	15	26	7	10
Avena barbata (slender wild oats)	2- 4	43	4	12	17	29	5	1
Cynodon Dactylon (Bermuda grass)	2-11	26	45	22	24	46	7	120
Spartina leiantha (cord grass)	6- 9	47	10	11	24	35	2	4
Distichlis stricta, laxa (salt grass)	5- 7	32	20	24	16	40	2	5
Poa annua (annual blue grass)	1- 8	25	+	15	18	33	1	3
Festuca megalura (rattail fescue)	2- 5	32	10	14	19	33	8	10
Bromus carinatus (Calif. brome grass)	2- 4	39	12	13	15	26	2	3
Bromus mollis (soft brome grass)	3- 5	37	19	17	15	32	6	10
Bromus rigidus (broncho grass)	4- 5	43	70	15	13	28	6	20
Lolium multiflorum (Italian ray grass)	3- 7	36	105	22	23	45	4	50
Lolium perenne (English ray grass)	3- 7	36	95	22	20	42	1-	7
Hordeum murinum (wall barley)	2- 4	39	17	21	12	33	5	7
PALMACEAE (palm family)								
Cocos plumosa (plumosa palm)	8-11	35				6	3	10
SALICACEAE (willow family)								
Populus Fremontii (Fremont cottonwood)	3	30	170	8	11	19	2	7
Salix lasolepis (arroyo willow)	2- 5	18	5			10	3	5
JUGLANDACEAE (walnut family)								
Juglans regia (English walnut)	4- 5	45	350	7	1	8	1-	4
BETULACEAE (birch family)								
Alnus rhombifolia	1- 2	24	300	1	1	2	1-	5
FAGACEAE (beech family)								
Quercus agrifolia (coast live oak)	3- 5	30	350	13	5	18	8	300
Quercus Engelmannii (mesa oak)	4- 5	28		15	7	22	3	70
Quercus dumosa (scrub oak)	4- 5	30	300	12	10	22	3	80
Quercus chrysolepis (maui oak)	5- 6	28					2	50
URTICACEAE (nettle family)								
Urtica gracilis, holoserica (creek nettle)	6- 8	15	9	11	3	14	1	4

*Franseria acanthicarpa = 100. See p. 28.

†See p. 28 for formula used in calculating importance.

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TABLE IV. PERTINENT DATA ON PLANTS OF IMPORTANCE IN POLLINOSIS IN SAN DIEGO COUNTY, CALIFORNIA

	Pollinating period (in months of year)	Pollen size (in microns)	Pollen produc- tion at maximum intensity*	Percentage of patients reacting			Plant abund- ance (Scale 1-10)	Import- ance (disre- garding toxicity**)
				1 +	2-4 +	Total		
POLYGONACEAE (buckwheat family)								
Rumex crispus (curly dock)	2- 4	25	21			18	2	5
CHENOPODIACEAE (goosefoot family)								
Chenopodium murale (nettle-leaf goosefoot)	3- 7	21	13	12	8	20	3	20
Chenopodium album (lamb's quarters)	4- 9	25	55	12	10	22	2	25
Chenopodium ambrosioides (Mexican tea)	7-11	21	+			21	1	2
Atriplex semibaccata (Australian saltbush)	5-10	18	+ -				5	3
Atriplex Breweri (lenscale)	8-10	19	75	13	7	20	1 -	7
Atriplex canescens (shad scale)	6- 8	25	60	14	3	17	1	8
Salicornia pacifica (pickleweed)	6-10	23	20	17	8	25	2	12
Suaeda californica (sea blite)	7-11	25	20	11	3	14	2	8
Salsola kali, tenuifolia (Russian thistle)	6-10	25	30	14	12	26	2	15
AMARANTHACEAE (amaranth family)								
Amaranthus retroflexus (rough pigweed)	6- 9	28	5	15	7	22	2	2
PLATANACEAE (sycamore family)								
Platanus racemosa (western sycamore)	3- 4	18	++	11	8	19	1	2
ROSACEAE (rose family)								
Adenostoma fasciculatum (chamise)	4- 7	17	20	13	7	20	6	30
LEGUMINOSAE (pea family)								
Acacia sps. (acacia)	1- 5	43		5	0	5	2	3
ANACARDIACEAE (sumac family)								
Schinus molle (pepper tree)	4-10	25	8	21	5	26	4	15
MYRTACEAE (myrtle family)								
Eucalyptus sps.	1- 8	25	1	11	4	15	4	2
OLEACEAE (olive family)								
Olea europea (olive tree)	4- 6	22	42	10	7	17	3	25
COMPOSITAE (composite family)								
Hymenoclea monogyra (desert fragrance)	10	21	135	17	11	28	2	15
Ambrosia psilostachya (western ragweed)	7-10	25	50	15	19	34	6	60
Franseria acanthicarpa (false ragweed)	7- 9	21	100	15	21	36	1 -	7
Franseria bipinnatifida (beach bur)	2-11	25	17	16	17	33	3	25
Xanthium pennsylvanicum (cocklebur)	7- 9	25	25	19	17	36	2	7
Artemisia tridentata, angusti- folia (sagebrush)	10	25	150	20	18	38	3	20
Artemisia californica (coast sagebrush)	10-11	21	40	14	34	48	16	90
Artemisia dracunculoides (Indian hair tonic)	7- 9	21	++	16	31	47	1	4
Artemisia Douglasiana (mugwort)	8-10	25	70	16	31	47	2	20

building. In Chart IV the pollen counts at the San Diego station for 1941 are given for comparison. Further explanation of Charts I to IV will be found under the section on "Interpretation of Charts."

The pollen included under the *Gramineae* (grass family) represent a particularly large number of species. In order to obtain some idea as to the grasses with which we were dealing and incidentally to add to our knowledge of the effect of the size of the grains on the ability of pollen to travel in the air, we measured every grass pollen grain found on our slides throughout the year 1941. Grass pollen counts, divided according to size, are shown graphically in Chart V. The sum of the daily grass pollen counts of each size group for the year 1941, is appended to Table I. Table II indicates the grass pollen grain which would fall within the arbitrarily selected size groups. It should be realized that the figures for pollen size represent averages, and that the actual diameter may vary as much as 5 microns either way from the figures given for the smaller sizes and as much as 10 microns for the larger sizes. Also there is a certain amount of overlapping in contiguous groups. This is indicated approximately by the brackets to the right in Table II.

In Table III, the relative abundance, on a scale of 1 to 10, of each species of the plants of possible importance in pollinosis is recorded for each community in this county having a population of 1,000 or over. These values were determined by a careful survey of each locality at least every two or three months, over a period of four years. More frequent visits were often necessary in order to study some particular species. In addition, similar notes were made for the territories between centers of habitation. Both sets of data were considered in determining the values for each life zone and for the county as a whole. A "1-" indicates that the plant was present but not in sufficient abundance to be of any importance.

Table IV summarizes all of the remaining data necessary to determine the importance of each plant. The pollinating dates given are the results of direct field observations. They were compared with data given by Hall⁹, Piness, Miller and McMinn¹⁰, Rowe¹¹, and McMinn.⁸ Whenever marked differences occurred, the dates were carefully checked in succeeding years. It should be realized, however, that the pollination period for certain species may vary markedly from year to year depending chiefly on the occurrence of rains. Thus *Artemisia californica* (coast sagebrush), which usually pollinates in November, may do so as early as September or as late as January. Certain other dates are remarkably constant. For example, the onset of the pollinating season of *Hymenoclea monogyra* (desert fragrance) will rarely vary more than one or two days from the first day of October.

The pollen grain sizes were determined by actual measurement, the figures given representing average sizes. As already stated, the sizes of individual pollen grains of the same species may vary considerably. The fig-

ures compare fairly well with the measurements of Duke⁴, Wodehouse¹³, and Piness and McMinn.⁹

The amount of pollen produced by each plant was estimated in the following manner. The flowering heads from one square meter, or definite fraction or multiple thereof, of a pure stand of the species in question, were gathered as nearly as possible at the peak of pollination. The stems were placed in water in a quiet, sunny room, and glazed paper was spread beneath the flowers. After forty-eight hours the heads were shaken and the amount of pollen collected and weighed. At least two, and usually three, separate collections were made and weighed separately for each species.

The percentage of pollen-sensitive patients reacting to each species was determined by routine scratch tests. This total was subdivided into those slightly but definitely sensitive (one plus) and those strongly sensitive (two to four plus). Only one species (*Acacia*) failed to produce any strong reactions.

The figures for plant abundance are taken from the final column of Table III. These figures represent an estimate for the county as a whole and hence may be different from the figures for any specific locality or life zone as given in Table III.

The figures designating the importance of each plant were determined by calculation, using the formula already stated. The results of the calculations are given in round numbers so as not to give a false impression of accuracy. In a few instances the calculated result was modified if it seemed to conflict with known data from direct pollen counts, due regard to the volume of the pollen grains being given. In certain instances the value taken for "n" (the number of months of pollination) was less than the time indicated in the first column since the bulk of pollination for certain plants occurs during a relatively short time, sometimes only a few days, although the plant may pollinate lightly over a long period.

INTERPRETATION OF CHARTS

Field studies of pollinating dates, distribution of plants, and amount of pollen produced, together with a knowledge of the topography of the area and of the prevailing direction of the wind, enable us to interpret the various graphs in Charts I to IV with a fair degree of accuracy. The following remarks regarding the composition of the different groups should help to clarify the meaning of the charts.

Charts I, II and III.—*Populus* pollen comes from *Populus Fremontii* (Fremont cottonwood).

Fagaceae pollen comes chiefly from *Quercus agrifolia* (coast live oak) and *Quercus dumosa* (scrub oak) in San Diego, *Quercus agrifolia* in Escondido, and that species plus *Quercus Engelmannii* (mesa oak) at Alpine.

Oleaceae pollen is due entirely to olive trees since *Ligustrum* (privet)

which is of the same family can be differentiated microscopically and was counted separately.

Cupressineae comes from *Cupressus macrocarpa* (Monterey cypress) with perhaps a little *Juniperus californica* (juniper) pollen when the wind comes from the east.

Gramineae. The composition of this group should be apparent from a study of Chart V and Table II.

Chenopodiaceae and *Amaranthaceae* comprise a large group. However, studies of the importance of the various species (Tables III and IV) indicate that *Chenopodium murale* (sowbane) and *Chenopodium album* (lamb's quarters) make up the larger part of this group in the spring, with perhaps some help from *Atriplex semibaccata* (Australian saltbush); the remaining members of these two families account for the late summer and fall pollens of this group.

Ambrosiae must be due entirely to *Franseria bipinnatifida* (beach bur) in the spring, with the remainder of the group, chiefly *Ambrosia psilostachya* (western ragweed) contributing the fall contingent.

Artemisia. The early rise is accounted for by *Artemisia Douglasiana* (mugwort) with lesser help from *Artemisia dracunculoides* (dragon sage); *Artemisia californica* (coast sagebrush) accounts for the marked rise which occurs later.

Chart IV. *Schinus* comes entirely from *Schinus molle* (pepper tree).

Palmaceae is due chiefly to *Cocos plumosa* (plumosa palm).

Adenostoma and *Eucalyptus* are not related botanically although their pollen grains are identical morphologically except for size. It was realized too late in our study that these two could be differentiated fairly well by size alone and could have been plotted separately. However, most of the pollen represented by this curve in May, June, and July, comes from *Adenostoma fasciculatum* (chamise).

Chart V.—The meaning of Chart V should be apparent from Table II and the latter part of Table I.

Grass pollen grains under 31 microns in diameter come essentially from Bermuda grass. It is interesting to note that the peak comes in August and September rather than in the spring.

The group of grains from 31 to 40 microns in diameter is composed approximately of two parts *Lolium* pollen (ray grass, chiefly Italian ray grass), and one part that of other members of this group.

The group of grains 41 to 50 microns in diameter is dominated by those of *Bromus rigidus* (broncho grass).

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The group of grains over 50 microns in diameter is made up chiefly of *Avena fatua* (common wild oats) plus some *Spartina leiantha* (cord grass). It should be remembered that although the total number of pollen grains of the large sizes is small the amount of allergen present in each is, in all probability, proportionate to the mass of the granules. The volume of a grain of common wild oat pollen, for example, is ten times that of one of Bermuda grass pollen, that of Broncho grass is five times greater, and that of Italian ray grass, three times greater. Moreover, the number of pollen grains of the larger sizes present in the air is undoubtedly much greater at ground level than at the level of the roof of a two-story building where our slides were exposed.

DISCUSSION

Theory.—To adherents of the theory that testing and treating for the pollen of one species of a family is sufficient for all members of that family, this whole study will seem like "Much ado about nothing." It is not the purpose of this study to deal with that theory. However, one fact in our experience would seem to be an insurmountable obstacle to its acceptance. Many patients will react strongly to the pollen of *Cynodon Dactylon*, *Distichlis stricta* and *Spartina leiantha*, which are closely related grasses, and fail to react to that of all other grasses, whereas the reactions of certain other patients will be just the reverse.

Factual Data.—From Charts I, II, and III, it will be seen that on the whole, the amount of pollen is greater in Escondido than in San Diego and greater in Alpine than in Escondido. This is to be expected since the prevailing winds are westerly. The enormous values for oak pollen at Alpine may be somewhat deceptive, since, in spite of these high values, and in spite of moderately frequent skin reactions to oak pollen, proven cases of clinical sensitivity to this allergen are not common. Likewise, only a few cases of clinical sensitivity to cypress pollen have been found. The incidence of *Chenopodiaceae* pollen at Alpine in April, May, and June is high but since this pollen can come only from sowbane, lamb's quarters, and possibly some from Australian saltbush, which are not common in that locality, the pollen must be carried in by the wind. The rise in ambrosia-like pollen at Alpine during April and May is even more striking since this could come only from *Franseria bipinnatifida* or beachbur which grows only on a narrow strip of beach along the entire coast of California. Study of a relief map revealed the fact that a river valley extends from an area of the beach, where this species grows in great abundance, to Alpine and allows a clear sweep for a southwest wind to carry this pollen inland. No similar rise in this pollen curve occurs at Escondido because that city is protected from the beach by a range of hills to the west.

A study of Table III indicates that each locality presents a problem in itself. It is regrettable that data on many other communities had to be

omitted due to limitations of space. The western border of Balboa Park was taken arbitrarily as the dividing line between West San Diego and East San Diego. West San Diego includes Mission Beach, Ocean Beach and Point Loma. Coronado includes North Island and the strand which connects Coronado with the mainland. The area designated "mountains" actually includes the western and eastern foothills life zones as well. The coastal life zone might well be subdivided into the immediate coast comprising the beaches and salt marshes, and the area farther inland. Each has a characteristic flora and the treatment for a housewife living near the beach, for example, should be different from that for one living in East San Diego.

An example as to how the information contained in this study is utilized may be of interest. After determining a patient's pollen sensitivities by skin tests, we note the importance of the reacting species for the county as a whole from Table IV. We then consider from Table III the abundance of these plants in the life zone and also in the community in which the patient lives. In some cases it may be advisable to visit his home also, since species of no general importance may be quite important if they occur near the patient's residence, especially if outside his bedroom window. The ratio of the various pollens to be included in the treatment mixture is determined by the probable ratio of each in the atmosphere to which he is exposed, due regard being given to the degree of his sensitivity to each species.

Additional facts of interest concerning each plant species, which could not be presented in tabular form, are given in the supplement.

SUMMARY

1. A mathematical formula for determining the importance of a given plant species in pollinosis in any locality is proposed.
2. Charts of daily pollen counts for one year at three representative localities in San Diego County are presented.
3. The size of each grass pollen grain found on our slides during one year was measured and charted.
4. A botanical survey of plants of importance in pollinosis in this county is given.
5. The percentage of patients reacting to each species is given.
6. Data on the pollinating period, the amount of pollen produced, the size of the pollen grains, and the abundance of each species are given, evaluated by means of the formula, and correlated with the data referred to in points 2 through 4 of this summary.

We wish to acknowledge with sincere appreciation, the help of Dr. C. A. S. Kemper of Escondido and Misses Betty and Susan Noble of Alpine in exposing the slides, and of Mr. Frank Gander, head of the Botany Department of the San Diego Museum of Natural History, in identifying plant specimens.

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SUPPLEMENTARY DATA ON PLANTS OF REAL OR SUPPOSED IMPORTANCE IN POLLINOSIS, IN SAN DIEGO COUNTY, CALIFORNIA*

SPERMATOPHYTES (seed-producing plants, flowering plants)

GYMNOSPERMAE (conifers, cone-bearing plants, naked-seed plants, evergreens)

Pinaceae (pine family)

Pinus, sps. (pine tree)

Toxicity questionable. However, Rowe has reported a proven case of severe allergy to tamarack pine.

Cupressus macrocarpa (Lambertiana m.) (Monterey cypress)

A heavy producer of pollen but the toxicity is low. Nevertheless a few cases of proven allergy to this pollen have been found.

Juniperus californica (California juniper, "cedar"†)

Same comment applies as for the preceding species. In addition this species grows in the most thinly populated section of the county, namely the arid eastern slope of the Coast Range.

ANGIOSPERMAE (plants with enclosed seeds)

MONOCOTYLEDONES (one rudimentary leaf in the embryo, leaves usually parallel-veined)

Gramineae (Poaceae) (grass family)

Andropogoneae (beard grass tribe)

Andropogon saccharoides (beard grass)

Unimportant.

*All wind-pollinated species are considered of some importance unless otherwise indicated.

†Quotation marks enclosing common names indicate that the names are incorrectly applied.

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Sorghum halepense (*Andropogon h.*, *Holcus h.*) (Johnson grass, evergreen millet, Egyptian millet, St. Mary's grass, Cuba grass, Means grass, Aleppo grass, Syrian grass)

Roadsides and ditches.

Panicaceae (panic grass tribe)

Digitaria sanguinalis (*Panicum sanguinale*, *Syntherisma sanguinale*) (crab grass, "Devil grass")

Orchards and citrus groves. Said to be largely close-pollinated, hence probably of no importance. (Some botanists believe all grasses are self-pollinated to some extent).

Echinochloa crus-galli (*Panicum c.-g.*, *Oplismenus c.-g.*) (barnyard grass, barnyard millet)

A weed in cultivated fields, groves, and orchards.

Setaria lutescens (bristly foxtail)

Unimportant.

Phalarideae (canary grass tribe)

Phalaris minor (small canary grass, Mediterranean canary grass)

Much less abundant now than formerly.

Phalaris canariensis (canary grass, bird-seed grass)

Unimportant.

Agrostideae (bent grass tribe)

Stipa coronata (giant stipa, giant spear grass)

Dry slopes and mesas. A heavy producer of pollen but distribution is scant.

Stipa pulchra (*S. setigera*) (needle grass, nodding stipa)

Of minor importance.

Stipa lepidota (*S. eminens*) (small-flowered stipa)

Of minor importance. Note: no one of the genus *Stipa* is important but it is wise to include either the strongest reactor or a mixture of all three in the treatment antigen of patients reacting strongly to this group.

Polypogon monspiliensis (beard grass, annual beard grass, tawny beard grass)

In low places. Fairly abundant but pollen production is scant.

Agrostis alba (redtop, marsh or creeping bent grass, whitetop)

Large reactions are often obtained with this pollen, especially in patients who have lived in the East or in Hawaii but it is too rare to be of any importance in this county.

Aveneae (oat tribe)

Koeleria cristata (Koeler's grass, "June grass")

Rare.

Avena fatua (common wild oats)

Much over-rated as a cause of pollinosis. Abundant.

Avena barbata (slender wild oats, barbed oats)

A poor producer.

Chlorideae

Cynodon Dactylon (*Capriola Dactylon*) (Bermuda grass, "devil grass," scutch grass, wire grass, "salt grass" chicken foot, Indian couch grass)

Lawns and roadsides everywhere. The most important grass in pollinosis in this county. Said to pollinate chiefly at night. Pollinates all year but more in July and August in this vicinity. Some patients react only to this species, cord grass and salt grass and to no other grasses. *Spartina leiantha* (*S. foliosa*) (cord grass)

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Occurs as a pure growth in large salt marshes along the coast. Some pollen of its size was found on our slides during its pollinating season.
Chloris virgata (Rhodes grass)

Unimportant.

Festuceae (fescue tribe)

Distichlis stricta, laxa (*D. spicata*) (salt grass)

Abundant only in salt marshes along the coast. A dioecious grass. Sometimes mistaken for Bermuda grass but the flowering head is entirely different.

Dactylis glomerata (orchard grass)

Unimportant although many patients react strongly to it.

Lamarkia aurea (*Achyrodes a.*) (golden top, toothbrush grass)

Most of the florets are sterile and hence produce no pollen. Unimportant.

Poa annua (annual blue grass, low spear grass, six-weeks grass, dwarf meadow grass)

Lawns. Will flower when only one or two inches high so mowing does not eliminate its pollination.

Poa pratensis (June grass, Kentucky blue grass, spear grass, common meadow grass, green grass)

Occurs abundantly in lawns but practically none ever pollinates because it is kept cut, hence is of no importance. It will not grow in this vicinity without artificial watering.

Festuca megalura (practically identical with *F. myuros* and *F. bromoides*) (rat-tail fescue)

Hills and mesas throughout the county. The most abundant grass in San Diego County. The pollen production is rather scant however.

Bromus carinatus (very similar to *B. marginatus*) (California brome grass)

Waste places.

Bromus mollis (*B. hordeaceus*) (soft brome grass, soft cheat, soft chess, "poverty grass")

Abundant but much of it grows in fields with much taller wild oats and other grasses, so its pollen is not easily caught by the wind.

Bromus rubens (red brome, fox-tail brome grass)

A scant pollinator.

Bromus rigidus (*B. maximus*, *B. villosus*) (broncho grass, "fox-tail," rip gut)

The most important of this genus. The bromes taken together are fairly important. It is probably best to include a mixture of all four, in the approximate ratio of their importance, in the antigen of patients sensitive to this group.

Hordeae (barley tribe)

Lolium multiflorum (Italian ray grass, Italian rye grass, Australian rye grass, "darnel")

Abundant in all towns. An escape from cultivation. The most important grass, next to Bermuda, in this county. Very toxic. About 6 to 10 times as abundant as the next species. Makes a quick but coarse lawn.

Lolium perenne (perennial ray or rye grass, English ray or rye grass, red ray, red darnel, red dare, English blue grass, "darnel")

Very similar to the preceding but much less abundant.

Lolium temulentum (darnel)

Even less abundant than *L. perenne*.

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Hordeum murinum (wall barley, "fox tail," farmer's fox tail)

Pollen production fair.

Elymus triticoides (*E. orcuttianus*) (alkali rye grass, slender wild rye)
Unimportant.

Elymus condensatus (*E. cinereus*) (giant wild rye)

Canyons. Of slight importance.

Elymus glaucus (*E. americanus*) (western rye grass, glaucus wild rye)
Unimportant.

Palmaceae (palm family)

Cocos plumosa (plumosa palm, cocos palm, plume palm)

The most abundant palm. A feather palm. Reactions to its pollen are small and rare.

Phoenix canariensis (Canary-island date palm)

The role of this and other species of palm is doubtful.

DICOTYLEDONES (plants with two rudimentary leaves in the embryo, leaves with netlike veins)

Salicaceae (willow family)

Populus Fremontii (Fremont cottonwood, common cottonwood, poplar)

Along stream beds. Dioecious. The "cotton" has nothing to do with pollinosis.

Salix lasiolepis (arroyo willow)

Along stream beds. Dioecious. The willow pollens represent a transition stage between insect and wind pollination. The pollen is rather sticky. Several other species of willow occur but this one far exceeds all others combined.

Juglandaceae (walnut family)

Juglans regia (English walnut, Persian walnut)

Rare in this county. In regions where it is grown, sensitivity is sometimes severe.

Juglans californica (California black walnut)

Too rare to be important.

Betulaceae (birch family)

Alnus rhombifolia (white alder)

Only along permanent stream beds.

Fagaceae (beech family)

Quercus Kelloggii (California black oak)

A deciduous oak. Occurs at 4,000 to 6,000 feet elevation.

Quercus agrifolia (coast live oak, California live oak)

Throughout the county. Marked clinical sensitivity to oak pollen is rare.

Quercus Engelmannii (*Q. MacDonaldii*) (Engelman oak, mesa oak, "black oak")

Occurs at 1,800 to 4,000 feet elevation.

Quercus dumosa (scrub oak)

Common chaparral shrub.

Quercus chrysolepis (maul oak, canyon oak, gold cup oak)

Common in canyons in the higher eastern slopes of the mountains.

Urticaceae (nettle family)

Urtica gracilis, *holoserica* (creek nettle)

Along stream banks.

Polygonaceae (buckwheat family)

Rumex crispus (curly dock, yellow dock)

Low places. It is surprising that so little dock pollen was found on the slides since it is a good producer and the pollen is light.

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- Rumex conglomeratus* (green dock)
Unimportant.
- Rumex Acetosella* (sheep sorrel, sour dock)
Rare.
- Chenopodiaceae* (goosefoot, chenopod, pigweed, or saltbush family)
- Chenopodium murale* (nettle-leaf goosefoot, sowbane)
Road sides, orchards and waste places.
- Chenopodium album* (lamb's quarters, white pigweed, white goosefoot)
Common weed.
- Chenopodium ambrosioides* (Mexican tea)
Occasional weed.
- Atriplex rosea* (red scale, red orache)
Unimportant.
- Atriplex semibaccata* (Australian saltbush)
Pollen production scant but pollinating period is prolonged and the plant abundant.
- Atriplex serenana* (*A. bracteosa*) (bract scale)
Unimportant.
- Atriplex Breweri* (Brewer lenscale)
Along the coast especially at La Jolla. Sometimes used as a hedge.
Dioecious.
- Atriplex canescens* (*A. tetraptera*) (shad scale, wing scale, four-wing saltbush)
At Sunset Cliffs, Encinitas, San Ysidro and Jacumba. Dioecious.
- Salicornia pacifica* (*S. ambigua*) (pickleweed, samphire, glasswort)
Large areas in salt marshes along the coast.
- Suaeda californica* (*Dondia c.*) (sea blite)
Salt marshes along the coast.
- Salsola kali, tenuifolia* (*S. pestifer*) (Russian thistle, "tumbleweed," saltwort)
The most toxic member of this family. A tumbleweed.
- Amaranthaceae* (amaranth or pigweed family)
- Amaranthus retroflexus*, (rough pigweed, redroot pigweed)
Common weed in gardens and orchards.
- Amaranthus graecizans* (tumbling pigweed, tumble-weed)
Also a tumble weed. Pollen production so scant as to make its role doubtful.
- Cruciferae* (mustard family)
- Brassica campestris* (mustard)
Insect pollinated. Conspicuous but probably unimportant.
- Platanaceae* (sycamore family, buttonwood, plane tree family)
- Platanus racemosa* (western sycamore, California plane tree)
Common along stream beds.
- Platanus acerifolia* ("Oriental plane tree," London plane tree, cultivated sycamore)
Grown for shade.
- Rosaceae* (rose family)
- Adenostoma fasciculatum* (chamise, "greasewood")
The most common shrub in the chaparral. Insect pollinated but some pollen is carried by the wind. Pollen morphologically like that of eucalyptus but smaller.
- Adenostoma sparsifolium* (red shanks)
Eastern slope of the mountains. Pollinates later than chamise. Less abundant.

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Leguminosae (pea family, legumes)

Acacia (sps.) (acacia tree)

Greatly over-rated as a cause of pollinosis.

Euphorbiaceae (spurge family)

Ricinus communis (castor bean, castor oil plant)

May be of some local importance especially if near the patient's bedroom window.

Anacardiaceae (sumac family)

Rhus (sps.) sugar berry, lemonade berry, etc.

Unimportant.

Schinus molle (pepper tree, Peruvian mastic tree)

Insect pollinated but much pollen is carried by the wind also. Dioecious. (The trees with berries are harmless).

Rhamnaceae (buckthorn family)

Ceanothus (wild lilac)

Not a true lilac. Insect pollinated. Unimportant.

Myrtaceae (myrtle family)

Eugenia (sps.). Unimportant.

Eucalyptus (sps.). Insect pollinated.

Oleaceae (olive family)

Ligustrum (sps.) (privet). Occasionally of some local importance.

Olea europea (olive tree). Quite important. A transitional form between insect- and wind-pollinated forms.

Plantaginaceae (plantain family)

Plantago lanceolata (English plantain). Slight importance.

Caprifoliaceae (honeysuckle family)

Sambucus caerulea (blue elderberry). Questionable.

Compositae (composite or sunflower family)

Astereae (aster tribe)

Solidago californica (California goldenrod)

Insect pollinated.

Baccharis sarothroides (chaparral broom)

The pollen closely resembles ragweed microscopically.

Ambrosiae (ragweed tribe)

Hymenoclea monogyra (desert fragrance, single-whorled burrobrush, jecote)

Abundant in Mission Valley and other river valleys near San Diego.

Ambrosia psilostachya (western ragweed)

Roadsides and waste places throughout the county.

Franseria acanthicarpa (*Gaertneria* a.) (false ragweed, bur ragweed, false western ragweed, prickly ragweed)

Mission Valley and along the road from Buckman Springs to Jacumba.

Franseria bipinnatifida (*Gaertneria* b., *F. Lessingii*) (beach bur)

Abundant on the beaches all along the coast. Much ambrosia-like pollen occurred on the slides at Alpine in the spring which could only come from this species even though thirty miles away.

Xanthium pennsylvanicum (*X. canadense*) (cocklebur)

Common in low places.

Anthemideae (mayweed tribe)

Artemisia tridentata, *angustifolia* (*A. angusta*) (sagebrush, black sagebrush, wormwood, "sage")

Sagebrush should not be confused with sage which has nothing to do with pollinosis. Abundant from Descanso to Jacumba.

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Artemisia californica (coast sagebrush, hill "sage." California sagebrush, old man, wormwood)

Dominant shrub of hills and mesas near the coast. Pollinates very heavily for four or five days about three weeks after the first good rain in the fall. In the past seven years this period has come as early as October and as late as December.

Artemisia dracunculoides (Indian hair tonic, dragon sagewort, green sagebrush, tall wormwood)

Occasional roadside weed.

Artemisia Douglasiana (*A. vulgaris*, *A. heterophylla*) (mugwort, Douglas sagewort)

Along streambeds. This species has evidently declined in importance, probably due to the drying up of streams as a result of the construction of dams. Earlier writers classed this species as the most important cause of fall pollinosis in southern California. This is certainly not true now.

AN INTRADERMAL TEST FOR THE RECOGNITION OF HYPERSENSITIVITY TO THE SULFONAMIDE DRUGS. Leftwich, W. B., Bull. Johns Hopkins Hosp., 74:26, (Jan.) 1944.

Reports of sulfonamide sensitivity have varied from 2 to 36 per cent. Sulfathiazole is more prone to produce sensitization than are the other members of this group of drugs. Previous attempts to determine sulfonamide sensitivity prior to clinical administration have been unsuccessful. The present report is a study of seventy-six patients, thirty-eight of whom were thought to be clinically hypersensitive (eight were questionably so) and the remainder of the patients served as controls. Blood was withdrawn from patients who had been under treatment with one of the sulfonamide group for a period of at least five days, and whose blood level varied from 2 to 20 per cent mgm. This blood sample was checked carefully to assure sterility and a negative serology. A blood level below 1.5 mgm. per cent was found to be unsatisfactory for this investigation as was the serum from those patients who had been receiving the drug for less than five days. An intradermal skin test with this serum was compared to a serum control test injected at the same time. Reactions were of the immediate type, with no instance of delayed reaction. A total of twenty-one patients were found to be sulfathiazole sensitive; four were sensitive to sulfanilamide, three to sulfadiazine, one to sulfapyridine and four to sulfamerazine. This corroborates the statement relative to the frequency of sulfathiazole sensitivity. Of the thirty definitely hypersensitive patients, positive skin reactions were obtained in twenty-eight. In the control group only two showed positive reactions on skin testing. In only three of twenty-five hypersensitive patients were positive reactions noted to sulfonamides other than the offending drug. This shows that the skin test is relatively specific for the individual sulfonamide drugs. Skin tests on persons who had never received sulfonamide therapy gave negative reactions in twenty-seven of twenty-eight tests. The sensitizing antigen may be a sulfonamide plasma protein combination, occurring in the circulation of patients under treatment, the sulfonamide acting as a haptene. Hepatitis and hemolytic anemia as a result of sulfonamide therapy are thought by the author to be on a toxic rather than an allergic basis as two patients with these conditions failed to demonstrate positive skin test reactions.

L.J.H.

SOAP, SOAP SENSITIVITY AND SOAP SUBSTITUTES

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SOAP, which is the most universal, most successful, and psychologically the most acceptable of all detergents and cosmetics, is also one of the most ancient, its manufacture being described by Pliny and known before his time. Its many uses for toilet, household and industrial purposes probably make it also the most frequent skin contactant and, therefore, non-irritating as it may be to the majority of mankind, nevertheless one of the most common mild irritants. Used in normal amounts and on normal skin, soap rarely causes irritation but occasionally, because of its composition, chemical reactions or sustained use, its irritant qualities may cause a primary dermatitis. When the skin is abnormal, as in atopic eczema, it may act as a secondary exacerbating factor. The present paper concerns itself with a short history of the manufacture of soap, its chemistry, the nature of its action, the cause of its occasional deleterious effects, its germicidal activity, and the composition and use of some of the common soap substitutes.

In the days of Pliny (23-79 A.D.), soap was made by boiling goat tallow with beech ashes. The resulting soft potash-soap was treated with salt, becoming converted to a hard soda-soap. In later years, the wood ashes were replaced by soda ashes from seaplants and kelp, and in the thirteenth century, olive oil was substituted for tallow. In the eighteenth century, manufactured alkali began to be used, and later, coconut, palm and other oils, of which the most important constituents are: stearic, oleic and palmitic acids. At the present time, any oil may serve. Those of animal origin are tallow and grease, while those from vegetable sources include: coconut, palm, olive, castor, cottonseed, corn, linseed, and soya bean oils. The usual alkalis are: sodium, potassium hydroxide, and sodium carbonate, the reaction of the fatty acid and the alkali forming the salt of the fatty acid and glycerin.

In addition, among other substances, soaps may contain: potassium carbonate, trisodium phosphate, tetrasodium pyrophosphate, sodium sulphate, sodium silicate, calcium carbonate, persulphates and perborates, acid magnesium metasilicate (talc), barium hydroxide (barytes), ammonium hydroxide, rosin, essential oils, glycerin, starch, alcohol, sugar, organic and inorganic dyes, asbestos and kapok fibres, the last of these acting occasionally as an allergen in its own right.

Soaps may be medicated with sulphur, mercury, zinc, copper and lead, or with phenol, cresol, ichthyol and thymol. Although questionable in medicinal effects, soaps containing, among others, the following primary irritants

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are available commercially and used by patients: benzoin 5 per cent; boric acid 5 per cent; ichthyol 5 per cent and 10 per cent; phenol 1 per cent and 2 per cent; tar 3 per cent; resorcin 3 per cent and 5 per cent; salicylic acid 3 per cent; sulphur 5 per cent and 10 per cent; camphor 5 per cent; balsam of Peru 3 per cent; mercuric cyanide; metaphen; and organic dyes, bactericidal in action.

In industry, lime soaps form part of lubricating greases. The oleates, linoleates and resinates of the heavy metals, as aluminum, lead, cobalt and manganese, are used in paints, varnishes and water-proofing materials. Any of the above listed substances may, of course, act as primary or secondary, external or internal, irritating agents.

Since soap is hydrolized by water, the solution contains a precipitated acid or sodium hydrogen salt of the fatty acid together with small quantities of both the alkali and the free fatty acids. The water solutions are electrolytic conductors, and have been postulated by McBain²⁷ as containing "multiple charged, heavily hydrated, colloidal aggregates of ionized molecules." An alcoholic solution of soap acts as an unhydrolized, non-electrolyte.

Soap was originally thought to act because of its alkalinity. Spring⁴⁸ feels that soap acts as a "colloidal absorption compound." The extraneous material or dirt is given a lowered surface tension, and is therefore re-deposited with difficulty, being easily washed away. Particles of dirt may also be lubricated, made less adherent, dissolved and emulsified. Lewkowitsch and Warburton²⁵, in their excellent article, give the ideal cleansing concentration as a 0.25 to 0.5 per cent solution.

Many studies on the deleterious effects of soap on the skin have been done. These may be classified into three groups. The first, rarely reported, is the individual who, requiring soap in ordinary amounts, responds with skin irritation and does his best to limit his use of soap to a minimum. The second group includes housewives and launderers who may use soap a great deal in their work, or whose work requires the use of a strong, harsh or abrasive soap for purposes of cleanliness. The last group is limited to those whose exposure to soap may be great since they are concerned in its manufacture.

Jordon, Dolce and Osborne¹⁵ report on 239 instances of soap dermatitis in housewives and domestics. The skin condition improved in the warm months (when the skin was more acid), and during vacations. Patch tests were unsatisfactory because the materials were irritating, although in dilute solutions. Rabeau and Ukrainezyk³⁶, in a study of occupational dermatitis in laundresses, have shown that the skins of 90 per cent of them lacked the capacity for neutralizing alkali and at a level found in only 8 per cent of normal individuals. That the subject is controversial can be judged from the work of Klauder¹⁹ and his associates who believe that the soap is itself not irritating but that the essential oils, perfumes, dyes and rosins are the allergenic ingredients. Sulzberger⁵¹⁻⁵³, on the other hand,

states that almost any soap will give a positive patch test if applied for twenty-four hours in a solution stronger than 2 per cent. Such reactions, he says, are not allergic since they are paralleled by alkaline solutions of equal strength, and are due to the reduction of the normal capacity of the skin for neutralizing alkali.

Gattefosse and his collaborators¹¹ studied the skins of those of their patients who suffered from dermatological conditions, and divided them into three groups. For the first of these, the diseased areas were alkaline in reaction while the remainder of the patients' skin was of normal acidity. The second group consisted of patients in whom the skin, both healthy and diseased, was alkaline. The third group presented healthy and diseased skins abnormally low in pH, that is, acid. The pH of the skin was determined by colorimetric methods, using chlorothymoid blue as indicator. A drop of this material in contact with the epidermis or mucous membrane, or mixed with the secretions being examined, indicated a pH range of 5 to 7.5.

The dermatological preparations used in the treatment of these patients were made in accordance with the reaction of the patients' skin, acid mycoses being treated with a triethanolamine stearate preparation, the pH of which was 7.5.

Edwards⁸ tested the skins of human subjects with 0.0225 M solutions of pure and commercial soaps for four hours. Any irritations lasting more than two hours after the test was considered a positive reaction. His paper listed fifty-six soaps in order of irritating properties, and concludes that potassium soaps are more irritant than calcium soaps. Soaps made with lauric and myristic acids are more irritating than those made with pure acids.

Jordon and his associates^{15,16} performed 2,300 patch tests on 150 patients with eight widely-used toilet soaps, and two laundry soaps, in dilutions of 1:100 and 1:400. Fifteen of the patients with normal skins reacted to the dilute soap solutions. Jordon stated, therefore, that a positive patch test does not always signify a sensitivity to the substance causing it. On the other hand, approximately 50 per cent of those patients who presented dermatological lesions, reacted to the dilute soap solutions. Seven individuals with other forms of allergy gave four instances of reactions. The author feels that a mild erythema without papules or vesicles is not to be regarded as a positive reaction. He is of the opinion also that the alkaline content of the soap is of minor importance in the production of eczema; and that the fatty acids and other miscellaneous ingredients of the soaps are the most likely etiological factors.

Kooyman and Snyder²¹ discuss methods devised especially for the measuring of small differences in the mildness of soaps. They say that since soap is used in such large quantities, with so low an incidence of irritation, that it must be a very mild primary irritant. Secondary factors which produce hyper-irritability may include dry, ichthyotic skins and such environ-

mental factors as prolonged exposure to the sun, wind or cold and dry atmospheres. Controlled patch tests can, therefore, detect small differences in intensity of reaction. Of each soap solution, 2 c.c. are used to moisten the patch. The authors feel that the concentration of the soap should be great enough to produce some reaction, and had their greatest success in achieving such reactions with solutions containing 8 per cent by weight of soap. Under these conditions, the greater number of the subjects had a slight to moderate erythema after six hours of exposure. Soaps made largely from coconut or similar oils were more irritating than other toilet soaps. The test was able to magnify the effects of soap sensitivity objectively, and within a short period of time, the slight differences being of extreme importance to certain patients and under certain conditions.

Blank^{4,5}, at an earlier date, had discovered that the saturated fatty acids of low molecular weight gave more positive patch tests than those of higher molecular weight, and that the fatty acids in castor oil rarely gave positive patch tests. The higher the molecular weight of the fatty acids, the more alkaline must the skin be before the onset of irritation.

References to occupational dermatoses are many and voluminous. Excellent papers by Schwartz⁴¹⁻⁴⁶, Sulzberger⁵¹⁻⁵³, Klauder^{19,20}, Hall¹³ and Whitwell⁵⁶ discuss the incidence of occupational skin disease, stressing over and over again the rôle played by cleansing agents including soap which, in many cases, is the prime irritant.

The problem of soap dermatitis has also been worked upon from the point of view of the skin. Markowitz²⁶ masterfully summarizes the available literature, stressing the high acidity (pH 5.3) of the surface of the epidermis excepting "the scalp in children, and in adults the axilla, genitocrural folds, anal regions, interdigital spaces and portions of the soles." Blank^{4,5} found the antecubital region the most acid area on the arm, and Pillsbury and Shaffer³³ the fourth interdigital space of the foot the least acid area of the skin surface. They demonstrated that acid solutions applied to the skin had little tendency to rise in pH, but that alkaline solutions showed a definite and regular drop in pH. They conclude that a standard patch test is an inefficient means of maintaining the concentration of any applied solution.

Markowitz²⁶ quotes Marchionini as saying that alkalinity of the skin, by favoring coagulability of the colloids of the keratin layer of the epidermis, reduces their stability and resistance, and this, with the fact that certain bacteria and fungi thrive best in alkaline media, explains the frequency of microsporon infection in the scalps of children, of abscesses in the axillae of adults, epidermophyton inguinale and the yeast infections in the genitocrural and anal regions and the epidermophytids in the interdigital folds and certain parts of the sole.

Arnold¹, in a study of the relationship between certain physical-chemical changes in the cornified layer and the endogenous flora of the skin, demonstrated that the exogenous bacterial flora residing on the surface of the

skin can be increased by alkalization and by exposure to warmth. The same flora can be decreased by exposure of the skin to acid. The cornified layer behaves like a colloidal gel structure, an increase in water content causing an increase in the surface endogenous flora. Dehydration of this layer causes a decrease in the viable bacteria of the surface. The flora return to the normal density when the cornified layer readjusts itself, this adjustment requiring thirty minutes after alkalization and about two hours following acidification. The survival of the exogenous bacteria follows the same pattern, the increased water content of the cornified layer permitting exogenous bacteria to survive for longer periods of time. A dehydrated cornified layer rapidly renders bacteria non-viable.

Since soap is frequently used as a bactericidal agent as well as for cleansing, there are many studies concerned with these properties of soap itself. In this field also there is a lack of unanimity. In 1927, Barber and Noble³ found soap and water fully germicidal for *Staphylococci*, *E. coli*, and *B. subtilis*. On the other hand, Eggerth⁹ studied the effects of pH on the germicidal action of soap showing that it varied with the organism used. Walker⁵⁵ stated that ordinary soap solutions of a concentration of 0.4 to 0.6 per cent were equal to phenol 0.5 to 1.0 per cent, and rapidly killed staphylococci, meningococci, gonococci, pneumococci and diphtheria bacilli, while the bacteria of typhoid, paratyphoid and dysentery were killed by moderate concentrations of soaps made with saturated fatty acids.

Prescott and Riley³⁵ found each soap more effective against some bacteria than against others. Davison⁷ showed that soaps of high detoxifying ability and ready diffusion were highly germicidal as they were correspondingly poor surface-tension depressants.

In more recent years, there has been a complete reversal of this point of view. Klarrman and Shternov¹⁸ answer the query, "Are soaps germicidal?" by testing sixteen potassium, seven commercial, and six saponified fatty-vegetable oil soaps against: *Staphylococcus aureus*, *Streptococcus haemolyticus*, *Eberthella typhosa*, *Shigella paradysenteriae* and *Trichophyton rosaceum*, by the Food and Drug Administration methods, and found commercial soaps not germicidal. Pohle and Stuart³⁴ report, however, that some soaps will kill the organisms removed from the skin and that rosin soap used for one week reduces both residual and transient flora. Used at a pH of 10.2 and at 30° C., rosin soaps will kill *Staphylococcus aureus*, *Eberthella typhosa* and *Enterococcus coli*. Reasoner³⁷ some years ago apparently demonstrated the lethal effect of soap on the *Treponema pallidum*, and more recently Stock and Francis³⁹ have shown that soap inactivates the virus of influenza.

Notwithstanding the germicidal effect soap is supposed to have, germicides have been added to soap in an attempt to sterilize the skin. The history of these mixtures has invariably followed the same pattern. The material when in soap was not germicidal, and often caused a primary irri-

tation. The most recent, and probably the most promising, is described by Traub and his collaborators⁵⁴ who used a new synthetic phenol, designated as G-11. This compound, in soap, was found to be non-irritating to the skin as judged by more than 200 patch tests, repeated on the same subjects, ten to fourteen days later with negative results. Subjects using a 2 per cent solution regularly for one year showed no evidence of irritation. The regular use of the compound resulted in a lower residual count after two minutes of washing than could be achieved after twenty minutes of washing with ordinary toilet soap. The author concludes that a surgeon, or operating-room attendant, using this compound, could maintain an extremely low bacterial population of the skin, and perhaps shorten the pre-operative "scrub-up" procedures as well as eliminate the use of irritating germicides.

If soaps are germicidal, their effects may depend either on their composition or the changes they cause in the skin. From the work of Jones and Lorenz¹⁴ it would appear that calcium soap actually facilitates the production of staphylococcal infections since calcium ions, when present in an oil-water mixture, enable the contained bacteria to pass more easily into the oily layer and so into the follicles and the sebaceous glands; the bacteria being viable for at least two weeks in calcium soap precipitates.

Pillsbury, Livingood and Nichols³² state that it is the mechanical cleansing of the skin which is the effective means of reducing its bacterial inhabitants, being an important part of treatment of any superficial pyogenic infection. They go on to say that the strength that is ordinarily used in washing with commercial fatty-acid soaps is not antiseptic, and that the mechanical action of washing and scrubbing plays the more important part in lowering the bacterial counts. Potassium permanganate, boric acid and aluminum acetate were relatively ineffective in reducing the bacteria flora, suggesting that the solutions act by softening the skin so that the bacteria are more easily removed by washing and by other means. Arnold and his colleagues¹ feel that there is still another type of inter-relationship. The bacteria not killed by soap may be more easily killed by clean skin than by that which is dirt-contaminated. They discovered that although dirty skin had slight germicidal powers against *Salmonella enteritidis*, clean hands rapidly destroyed this test organism. For a general survey of soap in medicine, a recent article by Lesser²³ should be consulted. For an earlier, well-balanced discussion, that by Fantus¹⁰ is generally available and well worth reading.

It should be mentioned that soap is also used for other purposes than for cleansing and germicidal activity. In 1937, Nolan²⁹ described a method of using sulphur soap paste in the treatment of scabies. The material known as Sulphurfoam is widely used as a scabicide, the lather containing sulphur being permitted to dry on the skin, and renewed at the end of twenty-four hours. The patient with sensitivity to either soap or sulphur may react adversely to this treatment. More recently, Gordon and his col-

leagues¹² have used soap impregnated with tetra-ethylthiurammonosulphide—"Tetmosol." In eighty-eight of 110 men given three baths with 20 per cent "Tetmosol" in soap, the scabitic infestation was completely eliminated. In twenty-two patients, there was a relapse. Of 242 men given "Tetmosol" vaths, four developed a dermatitis, patch tests being negative in three of the positive reactors. It is difficult to evaluate in these patients whether the sensitivity was to the scabicide or to the soap.

Although not entirely pertinent to the present discussion, attention is drawn to a paper by Stokes, Lee and Johnson⁵⁰ on contact, contact-infective, and infective-allergic dermatitis of the hands. This paper represents a thoughtful analysis of 200 patients studied over a period of ten years, and discusses in detail the treatment of these coincident dermatitides of the hands of which soap sensitivity is only one part. The paper is unusual in its acceptance of the patient as an individual rather than as a case of dermatitis. Treatment is preventive and constitutional as well as local. To support the conviction that "disabled hands express bodily dysfunction preparing the way for, or reinforcing specific insult," the author concludes that "only by the broad, in combination with the detailed, approach can cause, treatment and the best prognosis the circumstances warrant be aligned on a sound foundation."

However controversial the literature may be on the cause or amount of soap sensitivity, the condition frequently exists and often complicates skin lesions not directly due to soap sensitivity. These must be recognized and treated, preferably prophylactically. The number of soap substitutes and the great amounts in which they are used prove how acute is the problem. Unfortunately, for hand cleansing, the ideal soap substitute has not yet been prepared, although some preparations are more satisfactory than others.

Schwartz⁴¹⁻⁴⁶ describes a sulphonated castor oil (pH 7.2) containing a wetting agent. The material has been used successfully, not only for cleansing, but also in patients in whom soap and water are contraindicated as in the treatment of atopic eczema in young children. Burkhardt⁶ advocates a similar preparation. Reuter³⁹, who lists a number of skin-protective ointments, suggests the use of a cleansing solution consisting of equal parts of sulphonated Neat's foot oil and mineral oil with gelatin 25 per cent added to white granulated corn meal, the proportion being 2:3.

Lane and Blank²² used sulphonated oils for 279 patients of whom 87 per cent improved and 8 per cent grew worse. Positive patch tests were given by 1 per cent. The patients' conditions relapsed when they returned to the use of soap. Rogers, Cohen and Goldberg⁴⁰ used sulphonated oils in

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the treatment of burns. The formula of their recommended preparation contained:

Paraffin and wax.....	265.00
Sulphonated mineral oil.....	330.00
Sodium laurel sulphate.....	10.00
Sulphonamide	50.00
Triethanolamine	100.00
Water	30.00

Mummery²⁸ discovered that the use of a neutral sulphonated castor oil in 2 per cent wetting agent, as a substitute for soap, decreased soap reactions from 12.5 per cent of 3,714 subjects to 5.7 per cent of 3,435 factory workers, and from 14.2 per cent of 572 to 3.5 per cent of 523 machine shop workers following its use for one year. The subjects were exposed to: paraffin, machine oil, cutting grease, and a number of chemicals which remove the oil present in normal skins. Extended use of the material left the hands soft, clean, and comfortable.

A number of authors suggest that the hands be placed in acetic acid 3 per cent after washing, in order to return its acid properties to the skin.

The most complete recent review (June, 1943) appeared in the *Journal of the American Medical Association*. It lists the thirteen formulas for protective creams and cleansing agents reported by Klauder^{19,20} and the protective applications described by Schwartz.⁴¹⁻⁴⁶

The difficulties attendant upon the use of these preparations are mentioned by Sharlit⁴⁷ who is critical of soap substitutes since they contain wetting agents which increase the permeability of the keratin surface of the skin and also hydrophilic oils which are occasionally irritating. Nether is psychologically satisfactory. He suggests the use of super-fatted soap containing at least 10 per cent of free vegetable oil. Kile¹⁷ suggests a practical solution, reporting on fifty-seven young women who used two soaps identical excepting for the super-fat content. Of the subjects, 86 per cent reported no discomfort of any sort with either soap. For the super-fatted soap, two registered some discomfort, but for the control soap, this number reached 12 per cent. Thirty per cent found no difference in the drying effects of either soap but 54 per cent found the super-fatted soap less drying than that which was not super-fatted. It appeared that the subjects with dry skins preferred the super-fatted soaps. Subjects with oily or normal skins seemed to prefer the control soap. Kile suggests that the soap may act by removing less oil from the skin than ordinary toilet soaps do, or perhaps that additional fat is left as a residue on the epidermis.

Sulzberger⁵¹, commenting editorially on a paper by Lane and Blank²², mentions the fact that the patients complained of a "dryness" of the skin following the use of soap substitutes. That this dryness is not an irritation was shown by Parkhurst³¹ who patch-tested patients with the oily residue left on the skin by sulphonated oils and sulphonated alcohol, and re-

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ported that they were not irritating, giving negative patch tests. In our own experience with patients suffering from soap sensitivity, this criticism is one of psychological value that the patient does not see the dirt removed and says that his hands and his body do not feel "clean."

Acidolate (National Oil Products) is one of the commonest used, commercially available sulphonated oils, described as being completely water-miscible independently of the temperature or the hardness or softness of the water. Containing fatty acids and of high molecular weight, it has emulsifying properties for both fat-soluble and water-soluble skin detritus. Its pH is 6.25 and approximates that of normal skin, and it therefore causes no alkaline reaction. Many of our patients are so accustomed to a lathering skin-cleansing material, however, that they object to any non-lathering skin detergent as a matter of habit and training.

A soapless detergent consisting of propylene glycol, propylene glycol esters, and sorbitol with a pH of 6.8 has proved quite satisfactory. No reports of sensitivity to this material have been recorded.

Of the lathering soap substitutes in cake form, two have recently been offered to physicians.

The first of these consists of lauryl sulphoacetate, diluted in betonite; the lather having a pH of 5.0 to 5.5. This soap is described as being non-irritating, and of low sensitizing index. Those of our patients for whom it was prescribed claimed that it was not an effective substitute for soap, although its cleansing properties were excellent. Their objections were purely psychological in type, but nevertheless firm.

On the other hand, six patients given the second soap substitute, which consists of sodium p-ter-octyl-phenoxy-ethoxyethoxyethyl ether sulphonate, lanolin, cholesterol and petrolatum, all remark on its efficacy. The material lathers, is emollient and detergent, with a pH of 5.5, being active in all types of water, including sea water. This preparation has only recently become available; no reports of sensitivity have so far been described.

It is apparent from this review, which is by no means complete, that soap sensitivity is an extremely complex phenomenon. Soap may cause irritation by nature of its primary or secondary constituents, or by its alkalinity, on skins which may be primarily or secondarily irritable by reason of their physiological condition, their allergic potentialities, concomitant disease and degree of exposure. Since the skin maintains its homeostasis, the changes in pH of the patch tests vary with the time of exposure. In addition, since the pH of the skin itself varies from site to site, this reaction is not constant. The evaluation of a positive patch test to soap is therefore difficult. The test itself is rarely dependable.

Soaps which are used for other purposes than cleanliness expose the patient to risk of additional irritation. Soapless detergents are available but none, as yet, is as satisfactory as soap.

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THE TREATMENT OF ASTHMA AND HAY FEVER. Robert A. Cooke, New York State J. Med., 43:1225, (July 1) 1943.

This comprehensive clinical review, though not directed particularly at the pediatrician, is very helpful because, in general, any therapeutic measure which will alleviate allergic conditions in adults will also be useful for infants and children. In view of the tendency of some pediatricians to discount casein as a cause of allergic manifestations, the brief case report of a physician with nasal allergy due to the ingestion of casein is most interesting. Atopic asthma is the type most frequently encountered in infants and children and young adults, and its onset is rare after the age of forty; infectious asthma may occur at any time from infancy to old age. Children up to eighteen years need little attention to the sinuses, if recurring infections can be controlled. The early removal of infected tonsils and adenoids is one of the best means of control. As sedatives in asthma, appropriate doses of codein or pantopon may be given children when necessary. If these drugs produce vomiting at first so much the better, for it is more effective than coughing in removing mucous plugs. For the definite purpose of producing vomiting in children, however, syrup of ipecac in doses of ½ to 1 teaspoon may be given. J.G.

REPORT OF A CASE OF SPONTANEOUS ANIMAL ALLERGY

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THE use of the terms *allergy* and *atopy* remains controversial when applied to the phenomena of altered specific reactivity occurring in lower animals. This additional report to previous literature on the subject should aid in a proper terminology.

The terms *allergy* and *hypersensitiveness* are used interchangeably to indicate all forms of acquired and specific altered reactivity in humans or in lower animals from that of the normal.

The authors agree with Sulzberger and others that, for instance, asthma, produced by quinine, is an allergy, whereas production of tinnitus by a dose of this drug, ordinarily not causing symptoms, would be an exaggerated response or hypersensitiveness. They also accept Forman's classification of allergic sensitivity as modified by Sulzberger and Coca's classifications of atopy.

However, after considering cases, such as reported by Wittich and his co-workers, and the facts herein reported, it is possible to give a new interpretation to Coca's concept of allergy.

Coca states in his classical manual (1933) that atopy means "certain clinical forms of human hypersensitiveness that do not occur so far as is known in the lower animals and which are subject to hereditary influence." We think that Coca has not denied the possibility of applying the word atopy to lower animals, since he did leave this possibility in his definition for the future, when the clinical form of hypersensitiveness, meaning quantitatively increased reactivity, may be proven to exist in lower animals.

From Coca's definition one does not infer that the lack of hereditary antecedents may be an element of fundamental judgment to discount a diagnosis of atopy. According to Ruiz Moreno's opinion, atopy is a diagnosis arising from a number of facts (mentioned by Coca) which in essence are the following:

1. Constitutional inherited conditions characterized as being fundamentally the result of smooth muscle spasm or Quincke type of edema.
2. Presence of personal conditions showing the same characteristics.
3. The clinical picture must be the result of the interaction between a substance like atopen, allergen or antigen with the specific antibody, as a consequence of prior tissue contact.
4. This reagin must be passively transferable and should not give reactions *in vitro*, such as precipitation or complement fixation.

The syndrome must be the result of a Quincke type of edema or smooth muscle spasm, in which one generally finds numerous eosinophiles either in the tissues, as in the blood, or in the secretions from

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the affected organs. Moreover, epinephrine should be an efficient sympathomimetic remedy in almost all the cases. These last facts reinforce the diagnosis of atopy. They support the four fundamental characteristics as secondary features. Furthermore, the first two fundamental characteristics mentioned lose their importance to the patient since their presence is secondary to the other two conditions.

CASE REPORT

The present case under study is a Cairn terrier dog, called "Betty," three years of age, weighing 20 pounds. Not long after birth, and almost to complete development, a syndrome developed characterized by a generalized pruritus. This became worse with a subsequent simultaneous erythema which persisted. At the time of the examination only dermal scratch lesions were observed. The idea that these lesions might be due to *Sarcoptidae* was discarded. After some time, skin lesions were observed on a congested erythematous site which was characterized by the presence of scabs of various sizes, yellowish brown in color, which desquamated easily. These lesions were spread on the folds but mostly on the belly and genital and peri-anal regions. Red-brownish scabs were also found, these being interpreted as being merely scratching lesions. In general, the pink skin became deep red with isolated spots of healthy skin. About a year ago, two plaques appeared on the dorsal posterior region at each side of the tail. These were of rough appearance, blackish brown in color, hairless, about the size of a silver dollar, easily removed and were thought to be of parasitic (fungi) origin. After staining some slides from the scratched plaque and plating two Sabouraud Petri dishes, we could corroborate the mycological involvement already suspected.

There was present a perennial rhinopathy, characterized by sneezing and a slight watery discharge.

The symptoms suggested a non-human spontaneous allergy. Accordingly, intracutaneous tests with various allergenic extracts were done on the anterior, previously shaved, thoracic region. Pertinent food allergens and routine epithelium and dust extracts, each with a total nitrogen of 0.05 mg., were used.

Positive results were obtained with the following allergens: maize (slight reaction), oats (slight reaction), cacao (slight reaction). As far as the inhalants are concerned, the dust extract, in a tenfold dilution, produced a slight positive reaction.

Considering the results obtained thus far, we did not continue with the routine tests. After two hours, the animal showed a typical symptomatic reaction with pruritus, erythema and reactivated eczematous lesions. Moreover, there was a generalized thrill and increased pulse, as well as increased respiratory rhythm with dyspnea and oliguria for about twenty-four hours. All these conditions obliged the animal to keep resting, and whatever foods or drugs were provided were refused.

A dose of 1.5 mg. of epinephrine was administered by the subcutaneous route, injecting 0.5 c.c. of 1:1000 solution each time. The animal completely recovered by this treatment.

Since the preliminary skin tests to meats were negative, we prescribed a meat diet. After a week, the suspected allergic symptomatology was pronouncedly improved by the elimination diet given. Moreover, the local skin treatment with iodine resulted in the improvement of the skin lesions.

We then performed the clinical counterproof with positive results. In order to corroborate our presumption about this case of spontaneous allergy, we carried on some laboratory tests. The animal was bled and the passive transfer test in a normal dog was performed with the serum.

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After forty-eight hours the presence of reagins in the serum of the dog under study was detected, since positive results were obtained after the same allergens were tested. Controls were negative.

Thereafter the serum was used for the detection of precipitins by two different methods as follows: 2.5 c.c. portions of serum in a series of three Kahn tubes were pipetted, to which 2.5 c.c. maize, oats and cacao extracts were added separately with a capillary pipette by the walls, each with a total nitrogen content of 0.05. Another series, using 2.38 of total nitrogen instead, was also set up, following the same technique.

Moreover, dust extract of two different concentrations, one being 1:10 of the second, was included in the first series of tests. With the same antigens and identical concentrations already mentioned, the following technique was used: 2.5 c.c. of allergen were pipetted first in the test tubes; then, the same amount of dog serum was added with a capillary pipette from the bottom. The whole set of tubes was observed after five, fifteen and thirty minutes, and no precipitation was noticed, even with the aid of a magnifying glass.

SUMMARY

The arguments which support our diagnosis of allergy in the lower animal, according to the terminology used by Coca and others, are the following:

1. The qualitative and quantitative acquisition of altered reaction.
2. The fact that the clinical picture is produced by nontoxic substances incapable by themselves of giving rise to the same symptomatology in the dog.
3. The curative action of an elimination diet, excluding the causative foods.
4. The fact that the administration of the causative foods gives rise to the above clinical picture.
5. The provocation of the clinical picture by the skin tests with extracts of the causative foods.
6. Diagnosis of anaphylaxis may be discounted, since we are dealing with a specific sensitivity spontaneously acquired, not proved by any treatment.

The supporting arguments for the diagnosis of atopy (atopy allergy) are the following:

1. Presence of transferable antibodies, other than precipitins (sensitizing antibodies).
2. Successful treatment with epinephrine.
3. The fact that we are dealing with a phenomenon due to the interaction of antigen and antibody.
4. Presence of smooth muscle spasm (dyspnea) and edema (rhinopathy and skin tests).
5. Positive skin tests with the causative food extracts.

CONCLUSION

This is one more case supporting the contention that the word atopy may be applied when referring to some forms of spontaneous allergy observed in lower animals.

SERUM POTASSIUM RESPONSE TO EPINEPHRINE IN NORMAL AND ASTHMATIC SUBJECTS

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SERUM potassium determinations on normal and asthmatic subjects have been made in an effort to demonstrate whether epinephrine given subcutaneously has any effect on serum potassium levels. There are conflicting reports in the literature regarding serum potassium response to epinephrine in normal human beings. Keys⁹ found that intravenous injections over a period of 1.5 to 3 min. of 0.005 to 0.3 mgm. epinephrine hydrochloride in normal man produced an immediate marked fall in the level of plasma potassium with a return to a near normal level in twenty minutes. This was followed in forty to sixty minutes by a rise which was in most experiments significantly above the pre-epinephrine level. Brewer et al.² determined serum potassium values in seven adults before and after rapid intravenous injection of 1 cubic centimeter of epinephrine 1:1000 into the opposite arm. They found values from 17.9 to 18.2 mgm. per cent before injection with rises to 19.1 to 22.4 mgm. per cent thirty to ninety seconds after injection of epinephrine. These values are in line with those originally reported by D'Silva⁴ in cat experiments in which the serum potassium rose more than 12 mgm. per cent above the original level one minute after intravenous injection of 0.05 mgm. epinephrine. Both Keys and Brewer were able to confirm D'Silva's results after rapid intravenous injection of epinephrine in dogs, cats, and rabbits. Flock⁵ found the continuous injection of epinephrine caused a decrease in serum potassium from 19 to 32 mgm. per cent in dogs. This has been confirmed by Larson,¹⁰ in cats and dogs by perfusion experiments.

Because, as Camp and Higgins³ have pointed out, both potassium and epinephrine in man as well as in animals show similarity in physiological response, potassium salts have been rather widely used in the treatment of allergic diseases. Attempts have been made to modify the course of bronchial asthma and other allergic disorders by altering the potassium-sodium relationship either by oral administration of potassium salts or by changes in potassium content of diet.^{1,7,12,13} The possible relationship between potassium metabolism and epinephrine action in asthma prompted the present study of the effect of epinephrine on serum potassium, using the drug in the doses and by the route in which it is so effective clinically.

EXPERIMENTAL STUDIES

The following studies were made on serum from both normal and asthmatic subjects. The methods determining potassium were those of Strauss¹⁴ and Harris.⁶ All determinations were done in triplicate. Serum

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital, Durham, N. C. Presented at the First Annual Meeting of the American College of Allergists, Chicago, Illinois, June 10 and 11, 1944.

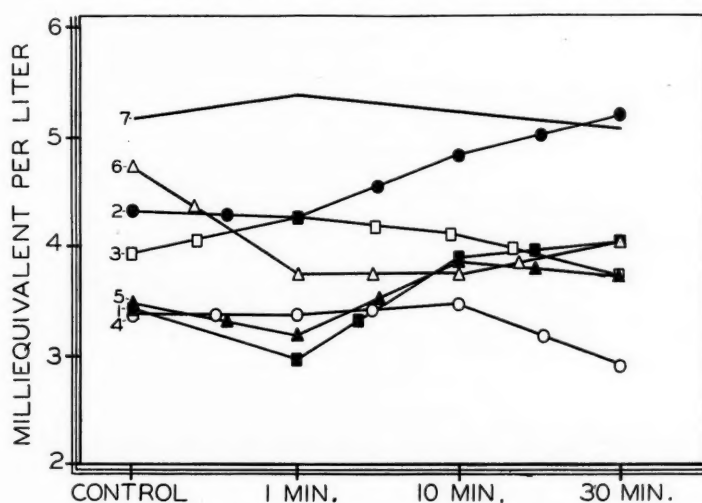
SERUM POTASSIUM RESPONSE—DEES

TABLE I. SERUM POTASSIUM VALUES IN NORMAL ADULTS AFTER SUBCUTANEOUS-PHYSIOLOGICAL SALINE INJECTION

No.	Name	Control Meq.	1 Minute Meq.	10 Minutes Meq.	30 Minutes Meq.
1	M.G.	3.43	2.96	3.89	4.08
2	N.B.	4.32	4.27	4.87	5.23
3	D.R.	3.91	4.28	4.13	3.73
4	A.M.	3.37	3.37	3.49	2.91
5	D.B.	3.49	3.19	3.85	3.73
6	O.A.	4.71	3.73	3.73	4.07
7	H.V.	5.19	5.40	5.28	5.10
	Mean	4.06	3.89	4.09	4.12
	S.D.	0.71	0.84	0.76	0.81

CHART I

SERUM POTASSIUM VALUES IN NORMAL ADULTS AFTER SUBCUTANEOUS PHYSIOLOGICAL SALINE INJECTION



potassium was determined on twenty-eight adults, eleven of whom had bronchial asthma. All subjects were either fasting or had been without food for at least six hours. The blood specimens were drawn before, and one, ten and thirty minutes after the rapid subcutaneous injection of 0.75 c.c. epinephrine hydrochloride 1:1000 into the opposite arm. The same amount (0.75 cubic centimeter) of physiological saline was used as a control injection. All subjects receiving adrenalin exhibited a rise in systolic blood pressure from 20 to 30 mm. Hg. with increase in pulse rate of

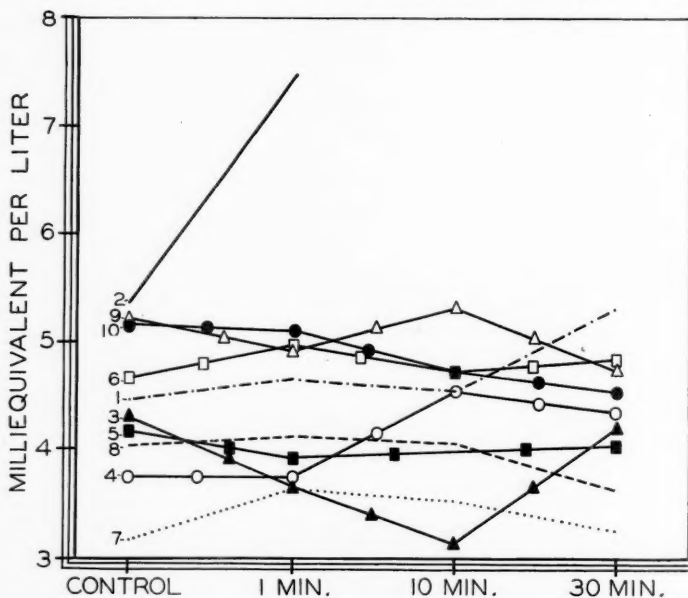
SERUM POTASSIUM RESPONSE—DEES

at least twenty per minute, one minute after the injection. Several patients with bronchial asthma, who were having attacks at the time of the experiment, showed transient relief of respiratory symptoms. The sera were divided into three groups (1) normal subjects after physiological saline, (2) normal subjects after adrenalin, and (3) asthmatics after adrenalin.

Table I shows the serum potassium values in the normal subjects receiving physiological saline injections, together with means and standard deviations for each time interval. Figure 1 shows a composite graph of these potassium values expressed as milliequivalents. Table II and Figure 2 give similar data for serum potassium after the injection of epinephrine

CHART II

SERUM POTASSIUM VALUES IN NORMAL ADULTS AFTER SUBCUTANEOUS EPINEPHRINE INJECTION



in normal subjects. The serum potassium values for the asthmatic patients before and after injection of epinephrine are given in Table III and Figure 3. Table IV shows the mean differences with their standard deviations for serum potassium values before and after injections in all three groups. In every case the standard deviation exceeds the mean difference, which therefore is without significance.

DISCUSSION

From these experiments it is shown that the subcutaneous injection of 0.75 c.c. of epinephrine 1:1000 does not produce any significant alteration

SERUM POTASSIUM RESPONSE—DEES

TABLE II. SERUM POTASSIUM VALUES IN NORMAL ADULTS AFTER SUBCUTANEOUS EPINEPHRINE INJECTION

No.	Name	Control Meq.	1 Minute Meq.	10 Minutes Meq.	30 Minutes Meq.
1	S.D.	4.48	4.67	4.55	5.33
2	S.W.	5.39	7.46		
3	S.W.	4.30	3.69	3.15	4.22
4	J.D.	3.75	3.75	4.54	4.36
5	S.D.	4.18	3.94		4.06
6	E.L.	4.66	4.96	4.72	4.84
7	S.W.	3.15	3.63	3.51	3.27
8	H.V.	4.02	4.11	4.06	3.65
9	M.F.	5.22	4.93	5.34	4.74
10	K.C.	5.18	5.13	4.73	4.57
	Mean	4.43	4.63	4.33	4.34
	S.D.	0.70	1.15	0.71	0.63

TABLE III. SERUM POTASSIUM VALUES IN ASTHMATICS AFTER SUBCUTANEOUS EPINEPHRINE INJECTION

No.	Name	Control Meq.	1 Minute Meq.	10 Minutes Meq.	30 Minutes Meq.
1	J.L.	5.95	5.87	6.05	5.99
2	F.P.	5.87	5.69	5.75	5.87
3	G.I.	5.39	4.73	4.31	5.33
4	M.S.	4.06	6.36		4.96
5	W.H.	6.54	7.15		
6	I.J.	6.61	4.73	5.39	
7	G.S.	5.51	5.84		
8	N.G.	5.74	5.35	4.73	5.09
9	G.A.	8.78	9.09	6.75	7.52
10	F.P.	7.39	7.58	8.12	6.73
11	J.McC.	6.37	4.24	6.87	5.87
	Mean	6.20	6.06	6.00	5.92
	S.D.	1.20	1.43	1.24	0.86

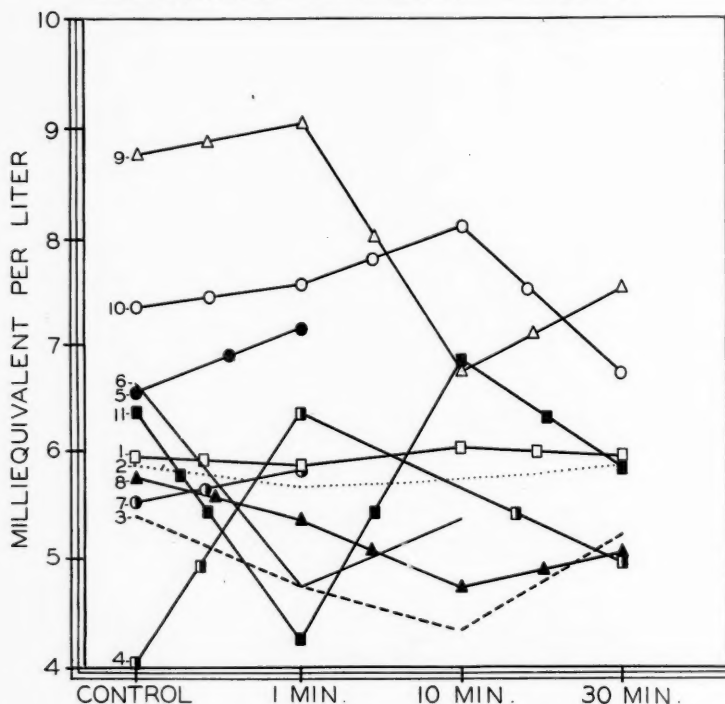
TABLE IV. MEAN DIFFERENCES BETWEEN CONTROL VALUES AND VALUES AFTER INJECTION, WITH STANDARD DEVIATIONS

	1 min.	10 min.	30 min.
7 normals-saline	-0.17 ± 0.45	+0.04 ± 0.51	+0.06 ± 0.40
10 normals-epinephrine	+0.9 ± 0.73	-0.02 ± 0.56	+0.01 ± 0.49
11 asthmatics-epinephrine	-0.11 ± 1.22	-0.52 ± 0.96	-0.27 ± 0.36

SERUM POTASSIUM RESPONSE—DEES

CHART III

SERUM POTASSIUM VALUES IN ASTHMATICS AFTER SUBCUTANEOUS EPINEPHRINE INJECTION



in serum potassium levels, as obtained from venous blood. This is at variance with reports in the literature after intravenous injection of epinephrine of an immediate rise or fall in the potassium levels and with statements as to an ultimate rise after thirty to sixty minutes to levels above the pre-injection level. In spite of absence of demonstrable chemical change in potassium, all of the subjects receiving adrenalin exhibited the typical subjective and objective physiological responses to the drug. That there is a definite relationship between the electrolyte level of potassium and the injection of adrenalin seems well established in experimental animals, and for humans when the route of administration of the drug is intravenous. This relationship is not borne out in the present series of patients using the subcutaneous route of injection. The exchange of potassium from extracellular to intracellular fluid may occur too rapidly or be of too small magnitude to be detected by the technique employed in these determinations. The assumption that the pharmacologic effect of epinephrine is due to increased mobilization of plasma potassium cannot

SERUM POTASSIUM RESPONSE—DEES

be demonstrated when epinephrine is given subcutaneously to asthmatic or normal humans.

In the present series of analyses normal sera in the control period gave mean values for potassium of 4.06 and 4.43 milliequivalents per liter. The group of asthmatic patients had a mean value for serum potassium of 6.02 milliequivalents per liter. This difference, using pooled normal, has a $t = 5.33$ for 27 degrees of freedom which is a highly significant difference. This finding is in accord with reports of Rusk et al.¹¹ and Jacobs⁸ of elevated potassium levels in allergic states as compared to normals. However, the values obtained in the asthmatics presented here are somewhat higher, and the differences between them and the normal are greater than in the two series referred to above. The explanation for the high potassium levels in our series may be related to the severity of the asthma, as all the patients were hospitalized for treatment of "status asthmaticus." The more obvious sources of high potassium such as diet and medication can be eliminated as contributing factors, since all the asthmatics were on general diets and were receiving no additional potassium when the blood samples were drawn. Technical factors likewise can be eliminated since the samples from asthmatic and normal patients were obtained under the same conditions, and the determinations were done simultaneously in both groups of patients.

CONCLUSIONS

1. Sera from twenty-eight adults, eleven asthmatic and seventeen normal subjects, were analyzed for potassium.
2. Determinations one minute, ten minutes and thirty minutes after subcutaneous injection of epinephrine, failed to show any significant alteration over the pre-injection serum potassium level in normal and asthmatic subjects.
3. The serum from normal subjects showed no alteration in serum potassium level after subcutaneous injection of physiological saline, at one, ten, and thirty-minute intervals.
4. There was likewise no significant difference between the values for serum potassium obtained in normal adults after injection of epinephrine or physiological saline.
5. The fasting serum potassium levels in asthmatic patients were significantly higher than in the normal subjects.

Acknowledgment: The author wishes to thank Dr. G. S. Eadie for the statistical analyses; also Susan S. Butler and Sarah W. Levy for technical assistance.

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USE OF SYNTHETIC DIET FOR FOOD ALLERGY AND TYPHOID. Olmsted, W. H., Harfond, C. G. and Hampton, S. F.: *Arch. Int. Med.*, 73:341, (April) 1944.

A diet composed of nutritional factors in chemically pure form is described for use in food allergy, typhoid and in differentiating food allergy from other GI complaints. Amino-acid mixtures supply the protein requirements, dextrose is the best source of carbohydrate, and the oils of cottonseed, corn and olive are available for the fat content. Salt mixtures and vitamins in pure form, round out this synthetic diet. The mixture of these substances may be made up in any desired volume and the caloric intake may be varied by feeding more or less of the suggested sample preparation: 70 grams amino acid, 140 grams of oil and 250 grams dextrose and 20 grams salt mixture. Vitamins are given separately. Since the taste of the feeding is unpleasant, a Levine tube is used for feedings at two to four hour intervals.

Nine brief cases of suspected food allergy are described and the results of the use of the synthetic diet are indicated and tabulated. In those cases where food was a definite cause of the symptoms, marked improvement was obtained. The diet has almost no residue. This synthetic diet can be given successfully and satisfactorily to typhoid patients in that it supplies adequate nutritional factors with a minimum of residue.

L.J.H.

ROUTINE TECHNIQUE OF ADMINISTRATION OF ANTIGENIC SUBSTANCES TO HYPERSENSITIVE PATIENTS

A Suggestion for Modification

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San Francisco, California

ALL textbooks on allergy contain instructions for the administration of antigenic substances to patients who are found to be sensitive on testing by the scratch method or the ophthalmic test, or whose sensitivity was revealed by systemic or constitutional reactions after injections of an unsuspectedly antigenic substance. I am referring especially to patients who are hypersensitive due to previous injection of the antigenic material. The following discussion does not apply to primarily sensitive patients, usually called atopic, such as patients with a history of sensitivity (asthma, urticaria, et cetera) to horse serum and dander; in these patients administration of the antigenic material seems entirely contra-indicated on account of the danger of fatal allergic shock, and every effort should be made to avoid such injections.

The usual instructions are based on desensitization of the patient by small increasing doses of the antigenic substance. The method is quite satisfactory, as ample experience demonstrates. The instructions include the advice to have adrenalin ready to combat undue reactions of hypersensitivity. I believe it is theoretically sounder and practically easier and safer to carry out the desensitization and the administration of the antigenic substance with the patient under the influence of a comparatively large dose and the sustained effect of adrenalin. For that purpose, I recommend the administration of one c.c. adrenalin in oil twenty minutes prior to the administration of the final dose of antigen. The least this technique will do is to minimize a general reaction. The most it may do is to prevent it entirely. Of course, it does not safeguard against the delayed type of shock; the patient will have to be watched for a suitable period of time.

This method is especially valuable for the administration of hormonal extracts to moderately and mildly hypersensitive patients in whom such injections are necessary for various reasons, such as: the administration of insulin in hypersensitive patients where acidosis or coma makes the desensitization, at the time, impossible or impractical; the administration of liver extracts in severe stages of pernicious anemia; the administration of hormonal substances which are inefficient or ineffective by oral administration such as extracts of anterior or posterior pituitary extracts, or androgens, estrogens or parathyroid hormones, or substances like diodrast.

This simple modification has proved a valuable addition to the technique of administration of antigenic substances to hypersensitive patients.

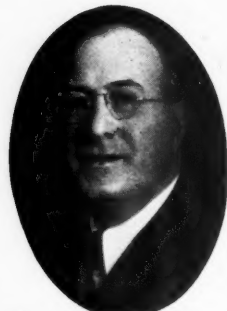
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ANNALS OF ALLERGY

Editorial

RESEARCH IN ALLERGIC DISEASE

Research in our special field is and must always be one of the most lively interests of the College. Yet we must confess our recognition of the limitations impeding organized attempts to implement this urgent interest.

The human creative spirit is an individual quality that functions best not in group effort but in solitude; the new ideas that are the stepping stones of cultural progress are usually born in a spiritual loneliness.

Although the formulation and the preliminary testing of an idea are originally activities of a single individual, the development of the idea for practical application requires, from the beginning, the co-operation of many others who, in turn, however, make their essential contributions, also individually. The relative value of these "developmental" researches is often difficult to assess. For example, the forgotten report of Roemer on the intracutaneous technique of determining small quantities of diphtheria toxin and antitoxin would have remained sterile but for Bela Schick; and had it not been for the great experiment of William H. Park in the control of diphtheria in New York City, as Schick himself remarked at the reception upon his arrival here from Vienna, there might never have been a Schick test. The test was "made" by Park's practical use of it.

Evidently, then, our endeavors to encourage scientific research in allergy must be directed to individuals, but we are sometimes none too sure that we are supporting the right project in the right way. We can only believe that any effort is likely to be better than none and hope that inscrutable chance may one day reward us.

In considering possible ways in which we might encourage profitable investigations, the rather hazardous notion came to mind of suggesting specific research-projects concerning a question of fundamental character.

The series of papers by Arthur F. Coca² on familial nonreaginic food allergy that we have published has not escaped the notice of our readers. It is a striking fact that notwithstanding the revolutionary nature of his reports, the meticulous documentation of all of his statements, and the personal interest that his findings must have for a large proportion of our readers, no attempt has been reported by a reputable allergist to refute or confirm his conclusions.

The only publications concerning this matter that have been made by others are those of Arthur Locke and his associates¹ and of A. Sumner Price³ (immunologist and pathologist, respectively), and we should point out that the conclusions of both of these reports are wholly in agreement with those of Coca.

EDITORIAL

Whatever our first impression may have been about this thesis, we believe it to be wrong to allow skepticism to prevent us from exploring the matter without prejudice.

We suggest, then, the following projects:

1. The application of the statistical method in an inquiry as to the non-reaginic allergic nature of "infectious asthma," chronic rhinitis, epilepsy, hypertension, gastric ulcer, and others of the list of symptoms to be found in Coca's monograph (Charles C. Thomas, publisher).

2. The first condition for such an enterprise is obviously mastery of the author's diagnostic method. This is at least a half-time job, probably of long duration, to be undertaken only by a wholly unprejudiced man or woman who has already adequate experience in allergy and also in the scientific method.

The statistical method discussed in this monograph is relatively uncomplicated, and a series of 100 or more cases, with an equal number of unselected controls, should provide sufficient data for acceptable conclusions.

3. The editors are interested to receive, at least for our information, detailed reports of cases that have been treated with this method. The entire pulse-diet record would be essential to an evaluation of the procedure.

If a sufficient number of satisfactorily completed case records should be received from several observers, we might see our way to prepare a joint publication of them.

We also offer our aid in enlisting Dr. Coca's suggestions to anyone who wishes to undertake one of the above-mentioned research projects.

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ADRENALIN AND RELATED SUBSTANCES IN BLOOD AND TISSUES. Raab, W., *Biochem. J. Lond.*, 37:470, (Oct.) 1943.

The author states that results obtained with accepted methods for the determination of adrenalin in blood and tissues are not due to adrenalin itself. Adrenalin-like substances containing a catachol nucleus as well as ascorbic acid will produce similar results. Shaw's method (described) can be used, however, for adrenalin determination even though its specificity is not for this one substance. L.J.H.

Progress in Allergy

A REVIEW OF RECENT MISCELLANEOUS LITERATURE

MAJOR LAWRENCE J. HALPIN, MC, AUS

Miscellaneous

Army Allergy. French, S. W., and Halpin, L. J.: Ann. Allergy, 1:1, 1943.

An allergy service, comprised of fifty-nine individual clinics, has been instituted in the Fourth Service Command, as of March, 1942. Preparation and standardization of pollen and other inhalent extracts have been completed at very low cost. All extracts are standardized on nitrogen content. Methods of investigation and therapy have been standardized so that each clinic is using the same method for recording reactions and instituting therapy. Tabulated reports from twenty-one clinics are presented. A total of 3,917 patients was seen in these clinics. These have been presented for discussion as follows: 1,269 patients with seasonal hay fever, 283 with seasonal bronchial asthma, 192 with seasonal hay fever complicated with bronchial asthma, 759 with perennial bronchial asthma, 770 with perennial allergic rhinitis, 350 with urticaria, 79 with migraine, 73 with gastro-intestinal allergy, 138 with eczema, 521 with food allergy.

Admission to allergy wards in hospitals was necessary in 1,153 instances. Of these, 820 (71 per cent) were asthmatic. An average of 18.1 hospital days was recorded for each patient. Only 195 patients seen on allergy service were eventually discharged from the Army because of the failure to respond to therapy; as compared to 267 that were reclassified to L. S. and maintained on duty.

The Problem of Allergy at an Army Air Forces Hospital. 1. Respiratory Allergy.

Hampton, Stanley F., and Rand, Harold: J. Allergy, 15:355, 1944.

Authors' summary:

1. A report of the activity of the Allergy Section and Clinic, AAF Regional Hospital, San Antonio Aviation Cadet Center, San Antonio, Texas, from August 1, 1942, to August 1, 1943, has been presented.

2. Eight thousand four hundred and nine clinic visits were made by Air Forces personnel to the Allergy Clinic of this Hospital.

3. One thousand five hundred and forty-one new patients were examined by the Allergy Section of this hospital.

4. Nine hundred and twenty-one of the 1,238 cases of allergic diseases were respiratory allergy (hay fever, vasomotor rhinitis and bronchial asthma).

5. One hundred and six or 8.9 per cent of the 1,191 men receiving the Certificate of Disability for Discharge under Section 2, AR 615-360 (Nov. 26, 1942) had allergic diseases. Eighty-six (7.48 per cent) had bronchial asthma.

6. Three and seven-tenths per cent of candidates for aviation training who were disqualified because of failure to meet the physical requirements (AR 40-110, Dec. 3, 1942) had allergic disorders.

7. The factors used in determination of fitness for aviation training of individuals with or suspected of having respiratory allergic disease are discussed.

8. The greatest problem of allergy has been *intrinsic* bronchial asthma associated

Major Halpin's work on the above Review was interrupted, and therefore this Review is not written in narrative form as are those which have heretofore been presented in THE ANNALS. To the carefully prepared abstracts of Major Halpin have been added some abstracts of articles published subsequent to the time when he was obliged to discontinue the assignment.

Secretary, Editorial Board

PROGRESS IN ALLERGY

with chronic respiratory infection. The high incidence of this syndrome in the young Air Forces age group is discussed.

The Significance of Allergy in Military Medicine. Gold, Edwin M., and Blazemore, James M.: *J. Allergy*, 15:279, 1944.

This is a report of the incidence of allergic diseases in a large Station Hospital and a method of pre-induction evaluation of the allergic state. Composite statistics are presented from January 1, 1942, to December 31, 1942. The disposition of all allergic patients is summarized. The length of service in the Army prior to the time of the patient's disability discharge is tabulated. It is shown that 65.9 per cent had less than six months' service prior to discharge, and 21.33 per cent had less than thirty days' service. Thus the importance of special allergy studies prior to induction on all patients with a history of allergy is emphasized. Criteria are presented when determining the disposition of soldiers as well as candidates for induction. The authors conclude that the universal use of pre-induction consultation service will eliminate needless waste of time and expense in initial training and subsequent disposition of the physically incapacitated soldier. They urge the adoption of standard detailed criteria when determining disposition of these patients and suggest a method of eliminating allergic inductees.

Army Allergy, Fourth Service Command, 1943. French, S. W., and Halpin, L. J.: *Ann. Allergy*, 2:365, 1944.

The authors reported on a total of 32,046 patients who had passed through sixty-seven allergy clinics in the Fourth Command for a period of one year. Included were 6,842 with poison ivy, 1,785 were civilian dependents of men in uniform, and the remaining 23,419 were military men. Eight thousand one hundred and thirty-nine patients were hospitalized on account of their allergies with a total of 172,455 days in the hospital. It is estimated that in this single Service Command the valuable services of 20,000 men were saved to the Army. There are now eighty-nine allergy clinics operating as parts of station hospitals in the Fourth Service Command alone. Medical men in charge of these stations are selected from a group specially trained in allergy procedures of testing and treating. The laboratory of the Command produces its own allergens and other materials for both diagnosis and therapy, supplying not only the eighty-nine clinics but many more in other Service Commands. Thus, uniformity of diagnostic and treatment procedures with standardized extracts on a vast scale makes for more accurate and uniform statistics.

The Allergic Problem of the Inductee, the Soldier of the Veteran. Shahon, Henry I.: *Annals Allergy*, 2:413, 1944.

1. The difficulties encountered by the examining physician of the Induction Board are discussed.
2. The important questions for the detection of the allergic manifestations in prospective soldiers are pointed out.
3. The allergic problem as encountered in the Army is briefly mentioned.
4. The benefits that honorably discharged veterans receive are amply discussed.
5. This question is still debatable, namely: How is the Rating Board specialist going to know whether the allergic disease existed prior to induction or enlistment? If at the time of such examination, the examiner finds that the physical examination is negative and that the history does not suggest the existence of allergy in the family, and the allergic tests if performed are negative, then it is safe to assume that the allergic disease or manifestation was not there at that time. If, later, this soldier develops any allergic disease, it can be said that it developed during service. Later, when this soldier is discharged from service, service con-

PROGRESS IN ALLERGY

nection for such a disability can be given. It is true that allergic diseases are not directly inherited and the tendency alone is inherited, yet no one can foretell the exact time of their appearance in life. It is possible that factors like overexertion, worry, exposure to cold or excessive heat, dampness, emotional strain and many others might precipitate the appearance of that hereditary tendency.

If, on the other hand, the allergic disease was present at the time of induction or enlistment to a degree hardly noticeable, and later it became greatly manifested with symptoms so disabling as to cause separation from the service, it can be said with some degree of certainty that this disease undoubtedly was aggravated by service.

Severe Urticarial Reaction Due to Pooled Human Plasma. Dickstein, Bernard: Ann. Allergy, 2:327, 1944.

1. The severe reaction of the patient was an allergic one due to elements specifically present in Pool 109 plasma and that these elements were antigens from milk, beef and lamb.

2. That no allergic reaction to human plasma *per se* occurred.

3. The chance of such reactions will be less if (a) blood donors avoid all food for at least six hours before giving blood, and (b) as many donors as possible contribute to a pool in order to dilute such allergens as might be present in individual instances.

Blood Studies in Allergy. I. The Direct Counting Chamber Determination of Eosinophils by Propylene Glycol Aqueous Stains. Randolph, T. G.: J. Allergy, 15:89, 1944.

A white cell diluent of phloxine and methylene blue dissolved in equal parts of propylene glycol and water permits the counting chamber differentiation of eosinophils on the same specimen used in determining the total leukocyte count. This technique has numerous advantages in comparison with previously described methods of enumerating eosinophils and would appear to be more accurate than the indirect method now in general use.

Blood Studies in Allergy. II. The Presence in Allergic Disease of Atypical Lymphocytes and Symptoms Suggesting the Recovery Phase of Infectious Mononucleosis. Randolph, T. G., and Gibson, E. B.: Am. J. M. Sc., 207:638, 1944.

The authors noted the similarity between atypical lymphocytes in the peripheral blood of allergic patients and those cells seen in the recovery phase of infectious mononucleosis. Inasmuch as both allergic reactions and infectious mononucleosis may produce symptoms of weakness, fatigue and lassitude the differential diagnosis is often difficult. The findings and impressions gained from a study of twenty-four allergic patients who had clinical manifestations of allergy along with the complaint of fatigue are reported.

Allergy in Relation to the Genito-Urinary Tract. Warrick, J. Thomas: Ann. Allergy, 2:396, 1944.

Allergy definitely must be considered as a cause of genito-urinary symptoms when they cannot be attributed to other causes, when they can be produced at will by the inhalation or ingestion of proven allergens, and when they can be controlled by withdrawal of the allergens. These symptoms may include frequency, painful urination with burning, tenesmus, nocturia, enuresis, ureteral colic, dysmenorrhea, leukorrhea, vulvar and genital irritation, and uterine contractions to the extent of terminating a pregnancy.

The rarity of genito-urinary allergy is understood, and evidence should be carefully weighed before a definite diagnosis is made. The diagnosis is substantiated

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by other frank allergies in the personal and family history, but it should be made only by exclusion and after therapeutic trial. The cases presented offer substantial evidence of genito-urinary allergy as the explanation of the symptomatology.

The possibility of an allergic reaction in the genito-urinary tract must be considered in the treatment of pregnant women. Reactions to serum or ragweed hypsensitization may cause abortions or premature labor.

Experimental work substantiating the fact that the tissues of the genito-urinary tract manifest a frank allergic or shock reaction is cited.

Close co-operation of the allergist and urologist is necessary if genito-urinary allergy is to be ruled out or, if proved, to be properly managed and results obtained.

Carbon Dioxide by Inhalation as Expectorant. Banyai and Cadden. JAMA, 123:1078 (Dec.) 1943.

Banyai and Cadden studied the clinical use of carbon dioxide inhalations in tuberculous patients. A mixture of 10 per cent carbon dioxide and 90 per cent oxygen administered by the closed method through a mask, or by the open method through a glass tube, is well tolerated. The relief obtained is noticed subjectively and objectively: spells of strenuous, exhausting coughing are prevented and thereby rest is secured for the patient and particularly for the lungs; an unproductive cough is transformed into a useful one; directly after inhalation the amount of expectorated sputum is increased and its character changed from a heavy, thick and tenacious type into a thinner, serous and more watery kind; the use of expectorant drugs and narcotics can be reduced.

The effectiveness of carbon dioxide is attributable to the facts that (1) it is a powerful respiratory stimulant and it induces increased inspiratory movements of the thorax, which in turn cause a stretching and dilatation of the bronchial tubes; (2) it stimulates the myoelastic structures of the lung and leads to a forceful peristaltic movement of the bronchi; (3) it liquefies mucopurulent inflammatory exudate that stagnates in the bronchial tract. The treatment is indicated whenever there is an accumulation and retention of inflammatory exudate in the bronchial tract and its evacuation, in spite of strenuous cough, is inadequate. The treatment should not be given to patients who have had recent pulmonary hemorrhage; to those with severe emphysema; when extensive pulmonary fibrosis is present without atelectasis, bronchiectasis or mucopurulent retention in the air passages; to patients with acute plastic pleurisy and pleurisy with effusion; to hypertensive patients, and when the cause of cough is outside the lungs.

Hypersensitivity from Inhalation of Atomized Fluid Antigens. Hopps, H. C., and Moulton, Stanley: JAMA, 123:1051, (Dec.) 1943.

Inhalations of finely atomized specific antiserum have been suggested for the prevention and treatment of influenza. A possible hazard of this experimental procedure has just been recorded by Hopps and Moulton. Their report is based on tests made with five antigens (nonhomologous) on guinea pigs and rabbits. The animals were placed in a closed chamber and exposed for twenty minutes to finely atomized particles of the various serums. By the third of the three weekly exposures many mild reactions were observed. By the fifth week of such treatment allergic reactions were severe. Several of the sensitized animals died in the chamber during exposure to the atomized specific antigen. Since serious allergic reactions and fatal anaphylactic shock have occurred in animals from a procedure which has been suggested for human beings, further human studies should be pursued with great caution. Routine use of aerosols of this nature is not now desirable.

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Instructions for Venipuncture and Intravenous Therapy. Lundy, J. S., Adams, R. C., Seldon, T. H.: Proc. Staff Meetings Mayo Clinic: 19:152, (Mar. 22) 1944.

Standardization of intravenous equipment for institutions is advised. In the procedure of venipuncture, the use of local anesthetic is recommended so that patient may have painless management. If the vein is small, insert needle with bevel down; if large vein, bevel may be up. Failure to utilize many available veins (in hands) and failure to take measures (moist heat applications) which cause full vein distention are cited. Tourniquet about 1 to 1½ inches above site of venipuncture produces the best distention of veins in that region.

Venipuncture in Presence of Edema. Schwartz, Steven O.: J. Lab. & Clin. Med., 28:1629, 1943.

A method of easy venipuncture in presence of arm edema is described: Place the thumb over antecubital space and exert pressure for 30-60 seconds with pitting produced. Antecubital veins stand out in bottom of "pit" since fluid has been expressed from both overlying tissue and that of the surrounding veins.

Use of a Nebulizer to Produce Oxygenated Vapor: Report of Case of Acute Laryngotracheobronchitis. Albers, G. D.: Proc. Mayo Clinic Staff Meetings, 18:511, (Dec. 29) 1943.

Acute fulminating laryngotracheobronchitis in childhood demands early tracheotomy and the administration of adequate moisture and oxygen. This crust formation and toxemia can be abated. The author describes the use of a nebulizer containing water through which pure oxygen is passed. The nebulizer is attached to the tracheal tube and adjusted to permit an adequate flow of oxygenated vapor. Necessary parts may be assembled from available oxygen apparatus. Case report.

Possible Etiology of Appendicitis. Dutton, L. O.: Ann. Allergy, 1:17, 1943.

Certain abdominal complaints of allergic origin may simulate a surgical condition. Dutton presents a clinico-pathological concept of appendicitis which accepts allergy as a fundamental etiologic factor. Such a consideration clarifies many points for an otherwise confused etiological situation. 123 consecutive cases of appendicitis were studied with clinical diagnosis as follows: acute 77, subacute 19, chronic 27. The pathological diagnoses were varied and showed little correlation between symptoms and pathological findings.

Without mechanical factors, only edema can account for obstruction. Dutton believes this functional edema to be allergic, inasmuch as this edema, capillary congestion and eosinophilic infiltration are reversible and similar to allergic tissue response. Throughout this series of cases these features of allergic reaction were seen in various degrees. A history of allergy was obtained from 87 of these patients, of whom 45 had had hay fever, asthma or urticaria. The author's presentation pertains to allergic reactions leading to appendicitis; not to symptoms simulating appendicitis. He recommends continued practice of treating appendicitis as a surgical disease; even though the allergic considerations may be sound and valid.

Observations on Bacterial Allergy in Scarlet Fever. Conner, James A., and Milzer, Albert: Illinois M. J., 84:214, 1943.

The authors believe hemolytic streptococci may be implicated in the appearance of urticaria in patients convalescing from scarlet fever. There was elevated temperature associated with these skin lesions. Urticaria showed late occurrences in the disease (eight to twenty-six days). All three cases presented were those of uncomplicated scarlet fever. Patient one had two previous attacks of scarlet fever. There was urticaria with the second attack although the patient had received no convalescent serum. Positive skin tests were obtained with cultures from the throat.

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Skin reactions are separate and distinct from Dick toxin results. One should consider the possibility of correlation of streptococcus allergy to delayed or late hemorrhagic nephritis and nonsuppurative arthritis. Most cases in the past were thought to be due to serum or food, or drug. Case reports.

New Interpretations of the Allergy Cutaneous Test. Stoesser, A. V.: *J. Lancet*, 64:145, 1944.

In a pediatric allergy clinic, the author found the puncture method of endermal testing to be productive of the best and most accurate results. It was determined that the multiple food reactions were of the greatest importance in eczema, with the reactions to dairy products being of particular significance. In allergic rhinitis, cereals, dairy products, and chocolate were most important. Meat, fish, or nuts deserved first consideration in the asthmatic child. Inhalant reactions increased in importance with the age of the patient to school age and puberty. Positive reactions to animal emanations, feathers and cottonseed were considered as of definite value regardless of the size of the reaction.

New Technique for Cutaneous Testing. Levinton, James: *J. Allergy*, 15:300, 1944.

In this preliminary report the author proposes a new method of skin testing. This is by means of an apparatus which consists of a dental drill, mounted on a small portable motor, similar to that used by engravers. This easily carried apparatus is used to peel the epidermic cells by means of slight friction when the allergic extract is applied to the rubbed areas in the usual manner.

Syringe Control in Passive Transfer Reactions Simon, Frank R.: *Ann. Allergy*, 2:15, 1944.

Perfect control of skin reactions has been afforded in passive transfers by the transfer control (testing site not previously sensitized with serum) and by specificity control (injecting extracting fluid into sensitized area). Simon adds "syringe control" to the above two. After thorough cleansing and sterilization, the syringe is partially filled with extracting fluid, which is brought into contact with all parts of the plunger and barrel of the syringe. Test sites of sensitized and nonsensitized skin are then injected with this fluid from this syringe. Equal and negative reactions then determine the acceptability of that syringe for further use with that particular serum.

Vascular Allergy. Harkavy, Joseph: *J. Allergy*, 14:507, 1943.

Sixteen cases of bronchial asthma have been observed since 1936. Four of these died and their necropsy reports are presented. All sixteen patients had chronic sinus infection which was regarded as a source of bacterial sensitization. Demonstrable reactions were noted on testing with staphylococcus, streptococcus and pneumococcus vaccine prepared from cultures of sputa and sinus washings. Food and pollen sensitivity were also responsible in seven of sixteen cases.

Clinically most all cases had similar histories and findings. Sterile pleural effusion had developed in eight cases, with eosinophilia 85 to 100 per cent in the fluid. Associated allergic manifestations varied from urticaria and purpura to polyarthritis and polyneuritis. Leukocytosis was present in most cases; marked eosinophilia in blood, bone marrow and serous fluids.

Detailed clinical, laboratory and necropsy reports were made of two male and two female deaths. Vascular lesions of particular import, characterized by marked eosinophilic infiltration, were found in the heart, lung and fibrous tissue. In one patient necrotic lesions in the liver and spleen were tuberculous to section, but no bacilli were found.

Characteristic perivascular lesions were present in the gastro-intestinal tract and kidney; the lesions in the latter organ entered the clinical picture in only one case

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causing hypertension and uremia. These vascular reactions are important in this symptomatology as evidence of allergic patients responding in a hyperergic manner to antigenic excitants. In bacterial allergy, symptoms may show up not only with direct infection, but with lighting up of old site, with toxins or with viruses. Various stages of vascular involvements were seen in same patient and in same organ. Venous involvement occurred in only one case.

Perivascular eosinophilic infiltration, necrotizing arteritis and periarteritis nodosa are hyperergic, exudative stage (reversible), while endarteritis obliterans and vascular fibrosis are anergic (irreversible). Eosinophilia is noted inversely to the degree of anergy. Harkavy considers bronchial asthma to be an expression of a hyperergic vascular response and accompanying vessel changes not representative of disease entities, but rather qualitative and quantitative degrees of hyperergic and anergic reactions. The heart in bronchial asthma may be normal, hypertrophied or directly involved as part of the hyperergic vascular response. Early diagnosis, correct therapy, change of climate, et cetera, in this type of asthma may bring about reversibility of hyperergic responses.

Lessened Sensitivity to Tuberculin in Acne. Lynch, F. W.: Arch. Derm. & Syph., 49:174, 1944.

The author shows that of 13,748 students, 3,549 had positive reactions to the Mantoux test and 3,997 had acne. Over a three-year period, positive Mantoux tests were found more often in absence of acne than when acne was present. Data given suggest that there is lessened sensitivity to tuberculin in persons with acne.

Canine Sensitivity to Ascaris Antigen. Brunner, M., Altman, Irving, and Bowman, K.: J. Allergy, 15:2, 1944.

Dog and pig ascaris antigen was used for intradermal testing on 24 dogs. Positive cutaneous reactions were obtained in 50%. Constitutional reactions from skin testing were noted in two dogs, both of whom had had previous nematode infection. Evidence of skin sensitizing antibodies in the sera of these dogs was established with the appearance of positive passive transfer sites in four of five normal dogs and in six human subjects. The authors also present evidence of active sensitization with ascaris extract. These antibodies were heat labile, thus resembling human atopic reagins.

Relation of the Dose of Antigen to the Degree of Anaphylactic Shock in Dogs. Dragstedt, Carl A.: J. Immunol., 47:505, 1943. Abstracted in Ann. Allergy, 2:66, 1944.

Hypersensitivity: A Neglected Phase of Allergy. Bruck, Clifford F.: J. Mich. State Med. Soc., 42:10, 1943. Abstracted in Ann. Allergy, 2:345, 1944.

Diagnosis of Hydatid Disease. Bull. Lederle Lab., 11:29, 1943. Reviewed in Ann. Allergy, 2:185, 1944.

Allergic Phenomena in Relation to Abdominal Wound Evisceration. Henry, M. G.: Amer. Jour. of Surg., 54:118, 1944.

Allergic reactions must be considered in the question of evisceration etiology. It is admitted that generalized cachexia plays an important part in the production of wound separation; but evisceration does occur in normal, healthy, individuals. In a case reported, no semblance of chronic gut remained in the abdominal wound that had eviscerated on the fifth day post operation. This same patient had had complete healing of a thyroidectomy wound six months previously; at which operation no chronic gut was used. Had the suture material been defective, total and complete absorption would not have occurred in this short time. Twelve addi-

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tional cases were cited as further illustrations. The author suggests that a specific individual may be sensitive to the chromic gut used as suture material. These patients usually ail continuously from the time of the operation to the day of evisceration. There are present a low grade temperature, elevated pulse, distention, gas pains, and progressive ileus. The author believes there is some allergic substance produced in the wound which acts as a toxin to the patient, and dissolves the catgut more rapidly than normal, and which prevents normal healing. The source of the gut (sheep) is mentioned in the allergenic consideration.

A sample of chromic catgut was taken up into 1/10 N sodium hydroxide solution and used as a testing material on a series of patients. Negative reactions were seen in all of these except in the original case reported. Discussion is presented of the surgical considerations given to patients who have had evisceration.

Wound Disruption and Catgut Allergy: An experimental and clinical study, with a review of the literature. Pickrell, K. L., and Clay, R. C.: *Surgery*, 15:333, 1944.

The general and local factors are considered by the authors as of importance in wound healing. Of the former, malignancy, hypoproteinemia, vitamin C deficiency, age of the patient, and presence of debilitating diseases are briefly discussed. Local factors considered are debridement, method of placing sutures, presence of infection, the type of surgery, drainage, tension and strain on sutures, and the size and type of suture material. It has been stated that a patient may be sensitized to catgut by previous operations, by previous protein therapy or by previous treatment with sheep's serum. Sixty rabbits and eighty guinea pigs were used in the present experiments. Sensitization was attempted by various means, with both plain and chromic catgut. Negative results were obtained here, as well as negative skin test reaction with catgut extracts. Tests for anaphylaxis properties were negative in various experiments. Disruptions occur regardless of the type (catgut, silk or wire) of suture material used. Review of the literature with bibliography.

Tropical Eosinophilia. Kendall Emerson, Jr. U. S. Naval Medical Bulletin, 42: 118, 1944. Abstracted in *Ann. Allergy*, 2:341, 1944.

Relation of Spore Dimensions to Their Rate of Fall. McCubbin, W. A.: *Phytopath.*, 34:230, 1944.

Starting with the observed rates of fall recorded for 2-fungus spores, formulas are derived which may be used to calculate with a fair degree of accuracy the probable rate of fall of spores of several typical shapes and sizes, if the ordinary spore dimensions are known. For round or oval spores the product of the length and width in "u" divided by forty gives the approximate falling rate in mm. per second. (From Biological Abstracts).

The Pollen Content of the Air in Rio de Janeiro, Brazil. Greco, J. B., and Lima, A. O.: *J. Allergy*, 15:138, 1944.

Daily pollen counts were made in five sections of the city. Slides were coated with glycerine jelly and methyl green. There is only one pollen season in Rio; this lasts from the middle of May to the middle of June. Only one type of pollen is found existent—grass. *Melinis minutiflora* is chief source of the grass pollen. Average counts reached the peak of approximately 58 pollen grains per 1.8 sq. cm. at the end of May in 1941; and the peak of 40 in early June, 1943.

Pollen Studies in the Phoenix Area. Randolph, H., and McNeil, M.: *J. Allergy*, 15:125, 1944.

The climate in this area has a low humidity and lack of rainfall. Pollen counts are much lower than in the Middle West. Total count seldom was over 30 per cubic

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yard. Slides were coated with mineral oil or glycerine and exposed on a weather vane arrangement. Usual area covered is 1.8 sq. cm., representing one cubic yard of air. Authors recognize six families as the most frequent causes of hay fever: Graminae (grass), Compositae (composites), Amaranthaceae (amaranths), Chenopodiaceae (chenopods or goosefoots), Polygonaceae (buckwheat family) and Plantaginaceae (plantain family).

Pollen season begins in early February with cottonwood (2 weeks) and ash (6 weeks). Bermuda grass was noted in April and continued through the summer with a second rise in September. Rabbit bush (similar to ragweed) is important and begins in April and May. Beet-sugar pollen is important for those in the immediate vicinity. Carelessweed is important in August to November. Common ragweed is not found in the Phoenix area, and false ragweed is not numerous, but should be considered in October. Graphic pollen charts for 1934, 1935, and 1936 are presented.

A Note on a Possible Allergic Factor in Altitude Sickness. Baker, Julia: J. Lab. & Clin. Med., 29:831, 1944.

The author presents evidence to indicate the more common occurrence of allergic diseases at a higher altitude (Mexico City, 7,328 feet) than at lower ones. Case histories and data on 500 consecutive patients fifteen years of age and under have been reviewed in support of this contention. Of the 500 patients, 167 had severe hives or eczema. 100 of the 500 patients had diarrhea proven to be upon an allergic basis. Several typical instances are described. Baker feels that the anoxia of the high altitude may result in greater absorption and accumulation of protein products than at lower levels. Similar features are offered as an explanation of mountain sickness. Recommendations are made regarding avoidance of common offenders (egg, milk, wheat, etc.) and particularly the practice of overloading on any one food.

Weather and Death in Asthma. Petersen, W. F., and Vaughan, W. T.: J. Allergy, 15:97, 1944.

Several brief case histories and clinical pictures of fatal asthma are presented. All have been graphically (and in discussion) compared with temperature curves, the barometric pressure and the precipitation. In these cases, it is well demonstrated that the weather change preceding an asthmatic attack is usually that of falling temperature and that exitus occurs with subsequent rise of temperature. *Marked weather changes* and the body's physiological adjustment thereto are the important factors. If the combination of allergen, exposure, fatigue, infection, constipation, etc., is favorable to the development of an attack, the weather changes may become the determining factor. Other factors can initiate or accentuate the pendulation from one extreme state to the other. Among these factors besides weather are emotion, infection, physical activity, digestive function, endocrine (menstruation) and others.

Plasma Treatment of Severe, Near-fatal Anaphylactic Shock. Raynolds, Arthur H.: J. Allergy, 14:495, 1943.

Case report of reaction from pollen therapy. Diffuse swelling of arms, legs and face. Blood pressure 50 systolic with no diastolic heard. Epinephrine total 1.75 c.c. given in two hours. Weakness, nausea and itching persisted. Because of continued low blood pressure patient was given about 500 c.c. plasma. Discontinued because of chills. Blood pressure 96/60. Recovery. The author states intravenous plasma should be given early and in adequate amounts when there is excessive blood volume loss.

Successful Treatment of Extreme Allergy to Bee Body and Bee Venom. McLane, E. G.: Minnesota Med., 26:1061, 1943.

McLane reports a case in which marked sensitivity to bee body and bee venom was overcome with graduated injections of whole bee extract, followed by carefully

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spaced bee stings. Inasmuch as this extract protected the patient from both bee emanations and stings, the author suggests that there is likely a common substance present in both allergenic sources. Bibliography.

Brucella Allergy in Veterinarian. Huddleson, I. F.: M.S.C. Vet., 4:10, 1943-44.

It has been observed that the percentage of positive reactions to *Brucella* antigen in noninfected (symptom free) persons has a direct relationship to the opportunity for exposure to infected animals or materials. From what is known of veterinary practitioners, it can be predicted that 90 per cent of veterinarians who work with infected animals will become sensitive within two years if proper precautions are not taken. Sensitivity increases on repeated contacts. Rubber gloves and sleeves when working with *Brucella* infection are recommended as protection. Those exposed can prevent passage of most of allergen through unprotected skin by rubbing bovine blood serum having high *Brucella* agglutination titer (1-5000 or above) over that portion of skin in contact with infective material. The serum precipitates the antigen and delays or prevents absorption.

Philosophy of Scientific Investigation. Preface to *De l'anaphylaxie a l'immunité*. Arthus, M. (Translated by Sigerist, H.): Bull. Hist. M. 14:373, 1943.

The difference between fact and its signification is capital. Fact has an absolute value while the value of its signification is only relative. The fact is accepted by all, but the signification may vary with different scientists. The rigidity of fact can be contrasted with the plasticity of its interpretation: "It is good to find the different veins in a mine, but it is better to explore one thoroughly; the others constitute reserves for the future." In this preface to his book, the ardent experimentalist warns the reader to beware of theoreticians and theories. Preservation of independence and originality in scientific investigation is all important for success.

Importance of Dosage in Intradermal Immunization Against Transplantable Neoplasms. Gross, L.: Cancer Research, 3:770, 1943.

One hundred ninety-five mice were injected intradermally with 0.02 c.c. of sarcoma cell suspensions which varied in concentrations from 0.1 to 20 per cent. The minimum tumor dose capable of producing sarcoma was determined at 0.02 c.c. of 0.5 per cent strength suspension. Accurate dosage is of the utmost importance in tumor immunity, since acquired resistance can be overwhelmed with massive dosages.

Reactions to Parenteral Fluid Administration. Strumia, M. M., McGraw, J. J., Jr., and Blake, A.: Ann. Int. Med., 19:718, 1943.

Various causes for reaction are discussed. Classification includes: (1) Causative agents inherent in fluid alone (pyrogenic, nitritoid, embolic and mechanical). (2) Inherent qualities of fluid combined with condition of patient. Included here are hemolytic and allergic. The latter reactions are attributed to substances of alimentary origin contained in whole blood, plasma or serum to which the recipient is sensitive. Localized urticaria usually present, but may be generalized with angio-neurotic edema and rise in temperature. Asthma is occasionally seen. Edema of the glottis must be considered. This occurs in 0.3-1 per cent of the transfusions. One should insist that the donor be fasting. Patients respond well to epinephrine. True anaphylactic reactions are rare. (3) Conditions which are inherent in the recipient alone (hyperhemolysis, liver disease, hypoproteinemia, cardiac insufficiency). (4) Those due to temperature, air emboli, free hemoglobin, et cetera.

Biological Methods of Determining the Insecticidal Values of Pyrethrum Preparations (particularly extracts in heavy oils). Tattersfield, F., and Potter, C.: Ann. Appl. Biol., London, 30:259, 1943.

Insects are killed by being hit with particles of insecticide and/or by contact

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with a film of insecticide left on exposed surfaces. Evenness of the deposit is an important factor with oil media in the spray, because the medium itself is somewhat toxic. The same is true of the film technique, but it is more marked. The insect chosen for these tests was *Tribolium Castaneum* Hbst. The experiments were controlled as to dosage, insect, spray and film technique. Increasing the concentration was found to be more effective than increasing the deposit. No evidence was determined that the spray technique was better than the film exposure.

Vernal Conjunctivitis (Spring or Vernal Catarrh). Marton, Samuel: *Ann. Allergy*, 1:39, 1943.

The term is not satisfactory because the condition is not confined to spring, nor is the exudate catarrhal in nature. Clinically characterized by seasonal recurrence with symptoms confined to tarsal or limbal portions of conjunctiva. Acute stage characterized by redness, itching, lacrimation and mucoid discharge. The chronic form shows large papules on tarsal conjunctiva and the discharge changes to the lardaceous type. Chronic often confused with trachoma. The differentiating point is the history. If the onset is in the pollen season, with aggravation of symptoms during succeeding seasons, and with negative tests, a diagnosis of vernal catarrh must be made. Marton presents four cases of vernal catarrh in support of pollen as a prime etiologic factor. In treating the pollen dosages must be carried in high concentration.

Adrenalin and Related Substances in Blood and Tissues. Raab, W.: *Biochem. J.* London, 37:470, 1943.

The author states that results obtained with accepted methods for the determination of adrenalin in blood and tissues are not due to adrenalin itself. Adrenalin-like substances containing a catechol nucleus as well as ascorbic acid will produce similar results. Shaw's method (described) can be used, however, for adrenalin determination even though its specificity is not for this one substance.

An Association Between Red-Green Color Blindness and Some Cases of Asthma and Hay Fever. Molholm, H. B.: *J. Allergy*, 15:120, 1944.

Asthma and hay fever having onset before the tenth year shows a 2:1 majority for boys, suggesting transmission by sex-linked recessive factor. No difference in onset after tenth year. Red-green color blindness is definitely dependent, in all instances, on a sex-linked recessive factor. Of 357 male asthma and hay fever patients, 30 (8.4 per cent) were red-green color blind. This is about twice as great as for unselected males. Red-green color blindness was highest in those asthmatics without symptoms before 13 years. Similar, though not as marked, findings in the patients with hay fever. Only two red-green color blind persons were in a group of 67 with asthma appearing after 13th year. Indications are that hay fever in boys probably depends on a sex-linked recessive factor.

The Alaskan Species of Puccinella. Swallen, J. R.: *Washington Acad. Sci.*, 34:16, 1944.

Puccinella is a circumpolar genus of grasses well represented in Alaska. 13 spp. are described with key. The following new spp. are published: *P. grandis*, *P. borealis*, *P. globra*, *P. triflora*, *P. andersoni*, and *P. hulteni*. (From *Biological Abstracts*.)

Pernicious Vomiting of Pregnancy due to Sensitivity to Semen. James, D. W., and Wagoner, C. P.: *Int. Corres. Club Allergy*, 7:70, 1944.

The authors report a case of nausea and vomiting of pregnancy which is felt to be due to semen sensitivity. The use of a condom prevented subsequent episodes. The psychic factor was apparently ruled out in that the patient had possibility of

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semen sensitivity explained to her and on one occasion she was unaware of semen exposure. Passive transfer areas were positive on testing.

An Aid in Eliminating Dull Needles. Lundy, J. S., Adams, R. C., and Seldon, T. H.: Proc. Staff Meetings Mayo Clinic, 18:417, 1943.

A magnifying glass mounted on a ring stand permits the easy inspection of sterile needles in order that their sharpness may be determined without fear of contamination.

Allergy. Hughes, R. F.: Canad. J. M. Tech., 5:174, 1943.

In discussing general therapeutic considerations, the author mentions methods other than skin testing that can be used in instances of food allergy. These are chiefly elimination diets, leucopenic indices, pulse acceleration test, and food diaries. Hyposensitization to inhalent allergens has been successful. Oral desensitization to foods is recommended. Drug therapy in allergy is designed to stimulate the sympathetic system, since the effects of allergy are those of parasympathetic stimulation. Epinephrine is most suitable.

Periarteritis Nodosa; Report of Case. Lichtman, A. L., Stickney, J. M., and Kernohan, J. W. Proc. Staff Meetings Mayo Clinic, 18:500, 1943.

Illustrative case report. Histogenetically, there is necrosis of the media with resulting extension of the inflammatory reaction and repair into perivascular tissues. Subsequent infarction produces disability. Marked variation of vascular involvement is outstanding characteristic. Occlusion of vasa nervosum has been a constant observation of authors. Eosinophiles are usually present in the inflammatory reaction. Symptoms vary with the degree of involvement of different organs and tissues, depending on interruption of blood supply. Asthma (in 15 to 20 per cent), eosinophilia (often 70 to 80 per cent) and peripheral nerve involvement are common characteristics of periarteritis nodosa. The etiology is probably allergic or infectious with neither definitely proven.

Precipitation of Pulmonary Edema by an Overdose of Antigen in a Patient with Rheumatic Mitral Disease. Deissler, Karl J.: Ann. Allergy, 2:299, 1944.

Cardiac decompensation occurred in a patient with rheumatic mitral disease as a result of an overdose of pollen antigen. The mechanism of this occurrence and the therapeutic implications are discussed.

It appears that this occurrence represents a special form of cardiovascular complication of a generalized reaction to an overdose of antigen in a cardiac patient.

It is believed that this type of response should be distinguished from both the systemic and constitutional types of reaction both on account of the underlying mechanism and the therapeutic implications.

Immunity to Tetanus Induced by a Third Dose of Toxoid Three Years after Basic Immunization; Based on a Study of 38 Allergic Children. Peshkin, M. M.: Am. J. Dis. Child., 67:22, 1944.

Thirty-eight allergic children were given a "booster" dose of 0.5 c.c. combined alum-precipitated diphtheria and tetanus toxoid. This was done three years after their basic immunization. Mild reactions were noted in 33 per cent of the children. One systemic reaction occurred in a child given the combined toxoids. An average of two months after the "booster" dose, scratch-test reactions with these toxoids were negative. Adequate tetanus antitoxin titers were noted within one month in all cases. This titer was higher and more prolonged than that following the basic immunization. The author recommends the use of alum-precipitated tetanus toxoid alone for this "booster" dose in order to keep local and systemic allergic reactions at a minimum level.

(Continued on Page 90)

News Items

Dr. Maurice S. Fox announces the opening of an office for the diagnosis and treatment of allergic diseases at 223 American Bank Building, Vincennes, Indiana.

Dr. Lewis Palay, of Miami Beach, Florida, announces the opening of his office in the Medical Building, 541 Lincoln Road. His practice is limited to allergy.

Dr. Theron G. Randolph, formerly in charge of the Allergy Clinic at the University of Michigan Medical School, has accepted a part-time research position in allergic diseases at Northwestern University Medical School and has started the private practice of allergy in Chicago, at 700 North Michigan Avenue.

The contribution of Mr. Samuel Dorman, Long Beach, New York, to the Research Fund of the College, is gratefully acknowledged. Through Mr. Dorman, several other contributions to the Research Fund have been received, which were announced in the November-December, 1944, issue of the *ANNALS OF ALLERGY*.

Lt. Col. Boen Swinny, of San Antonio, Texas, who has been serving in the Armed Forces for four years, has been Commanding Officer of the U. S. A. Hospital Ship for about a year. Doctor Swinny's office has been functioning under the direction of Dr. Pearl Zink during his absence.

At the Seventh Annual Forum on Allergy, held at Pittsburgh, January 20 and 21, Dr. Mary Loveless of New York City was awarded first prize for the most meritorious work in the field of allergy appearing in the literature in 1944. Dr. Charles F. Code, Professor of Clinical Physiology, Mayo Foundation Graduate School of Medicine, Rochester, Minnesota, was awarded second prize. These prizes were made available through the Marcelle Award.

The fifth semi-annual refresher course in laryngology, rhinology and otology will be conducted by the University of Illinois, College of Medicine, at the College in Chicago, March 26 to 31, inclusive, 1945. While the course will be largely didactic, some clinical instruction will be included. This course is intended primarily for ear, nose and throat specialists. As the registration is limited to thirty, applications will be considered in the order in which they are received. The fee is \$50. When writing for application, please give details concerning school and year of graduation, and past training and experience. Address Dr. A. R. Hollender, Chairman, Refresher Course Committee, Department of Otolaryngology, University of Illinois, College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

1945 ANNUAL MEETING CANCELLED

The Board of Regents of the American College of Allergists, after consideration of all factors involved, officially announces the postponement of its second annual session, scheduled for Philadelphia, June 16 and 17. The action is taken this year voluntarily in order to co-operate to the fullest possible extent at the advice of the Office of Defense Transportation and in the interest of the nation's war effort.

A meeting of the Board of Regents will be held in June, at which time pertinent matters concerning the policies of the College to be instituted in 1945-1946 will be discussed and the various functions mapped out.

Plans are being made to hold an extensive instructional course in the fall at one of the Universities, and announcements concerning this will appear in the *ANNALS OF ALLERGY*.

★ *In Memoriam* ★

DAVID R. GODLIN

Dr. David R. Godlin, of Miami Beach, Florida, died July 27, 1944, at the age of forty-three years, in New York City. He received his M.D. degree in 1926 from Columbia University College of Physicians and Surgeons and interned at Christ Hospital, Jersey City, New Jersey. He opened an office at North Bergen, New Jersey, where he practiced medicine until 1939. He was attending surgeon at Christ Hospital, a member of the staff of Margaret Hague Maternity Hospital, both of Jersey City, and a member of the Hudson County and New York State Medical Societies, as well as the American Medical Association. Doctor Godlin specialized in surgery in New Jersey and later in allergy, having taken advantage of various intensive courses in allergy at Postgraduate Hospital, New York City.

He became ill in 1939, having suffered a heart attack. He left his practice in New Jersey and moved to Miami Beach to regain his health and opened an office at 541 Lincoln Road. While there he began a mold and pollen survey of the state. He was on the staff of Jackson Memorial Hospital where he conducted an allergy clinic.

He is survived by his wife, Rose Godlin, and a six-year-old son.

Doctor Godlin won the respect and admiration of all who knew him. His keen interest in allergy and the progress he made in this field is evidence that the College has lost a valuable member.

FRED W. WITTICH

HARRY IKER

News of the death of Mr. Harry Iker, of Chicago, an Associate Fellow of the College, which occurred February 19, was received just as this issue of *THE ANNALS* was going to press. A fitting tribute to him will be contained in a forthcoming issue of *THE ANNALS*.

THE EFFECTS OF DIET ON THE EAR, NOSE AND THROAT. McLaurin, J. G., Dallas, M. J., 30:24 (Feb.) 1944.

Mucous membrane of the nose and throat serves as a guide to the type of food eaten in excess by the patient. In the age group ten to twenty, lymphoid tissue is present in proportion to the absence of fats from the diet; in twenty- to thirty-year-old groups, catarrhal discharge depends on a deficiency of leafy vegetables in food selection, and in older patients a granular pharyngitis is dependent on an excess of cereals and foods prepared with white flour. The author divides the color appearance of the nasal mucous membrane upon a red and a pale syndrome basis. The red septum syndrome is found in those patients with chronic tiredness, constipation, irritable temperament and no appetites. They have a low tolerance for acid-ash foods. The pale septum syndrome is found in the allergic patients. Itching of the nose, polyps, subnormal temperatures, low BMR and hypotension are usually found. These cases are dependent on an excessive intake of alkaline-ash foods. A blood count and hemoglobin determination are important as aids in correctly establishing these color changes which are due to three factors: capillary size, change in the volume of septal tissue cells and the amount of interstitial fluid. The patient with constant post-nasal drip usually is an excessive user of sweet foods. Correction and dietary therapy in each syndrome is the addition of alkaline-ash or acid-ash foods in each particular instance.

L.J.H.

BOOK REVIEWS

A MANUAL OF SOIL FUNGI. By Joseph C. Gilman, Botany Department, Iowa State College, 392 pages, 135 illustrations. Limited edition. Price \$5.00. Ames, Iowa: The Collegiate Press, Inc., 1945.

Contents: Key to the classes, orders and families of soil fungi: Phycomycetes, Ascomycetes, Fungi Imperfecti and Mycelia Sterilia. The entire text consists of a succinct, orderly and practical taxonomic description, supplemented with excellent drawings illustrating genera. The distinguishing characteristics of the various classes, orders, families, genera, species and subspecies of soil fungi are adequately described. There is an authoritative global listing of the countries and states where the various species are found.

The manual is a revision, with the incorporation of a great amount of additional material, of a manuscript entitled "A Summary of Soil Fungi" by the author and E. V. Abbott. Although written primarily for workers in the field of soil microbiology, there was such a demand for reprints of the manuscript by men in industry and in medicine that the new publication was made available.

The text is not an exhaustive study of the techniques required for an investigation of soil fungi, but "to be helpful in identifying molds already in cultures." In this, the author has been very successful.

Since certain common air molds, all formed in soil, are the cause of allergic diseases, allergists are now required to have a basic knowledge of molds not only for practical application but for further investigations of the relative importance of fungi, when causing symptoms of hypersensitiveness.

Since the development of the latter state as a result of extrinsic factors depends upon the amount of contact with any excitant indigenous to the environment of the allergic patient, the states and countries in which these fungi are formed furnish a valuable supplement to aerial surveys of fungi already made by those interested in mold allergy.

All allergists interested in molds in relation to their specialty should avail themselves of this valuable manual.

F.W.W.

HAYFEVER PLANTS. Their Appearance, Distribution, Time of Flowering, and their Role in Hayfever, with Special Reference to North America. By Roger P. Wodehouse, Ph. D. (Lederle Laboratories). 245 pages. 73 illustrations. New and numerous tables. Series of Pl. Sci. Bks., vol. 15. Price \$4.75. Waltham, Mass.: Chronica Botanica Co., 1945.

This is an authoritative botany of hay fever by the author of "Pollen Grains," universally known by allergists. Contents: The Botany of Hay Fever; The Hay-fever Plants—Gymnosperms, Angiosperms, Monocotyledons, Dicotyledons; Regional Surveys; Glossary; Bibliography.

The first three chapters are devoted to pollens and pollination and the role that pollen plays in hay fever, as well as a description of all the plants known to cause hay fever, showing where they grow, when they flower and the characteristics which make them hay-fever plants. The last, or fourth chapter, is geographical, dealing with regional surveys with accurate and recent data on ten areas throughout the United States, besides Canada and Mexico. Numerous illustrations of plants and their pollen grains, mostly drawn by the author, are very informative and bring out details frequently lost by photography. There is a map of the ten hay-fever regions of the United States. The pollinating periods of hay-fever plants in these regions

BOOK REVIEWS

represent accurate, recent surveys, with the most important plants clinically printed in heavy type. The print throughout makes it very easy reading, and the arrangement is excellent for ready reference. The references to local surveys of others are very complete, and there is a discussion on hay-fever resorts.

The book is indispensable to all physicians interested in allergy when managing their local hay-fever problems, and it is the most complete authoritative text on the subject today.

Medical allergists will welcome this authoritative book on the flora, responsible for clinical hay fever and asthma, indigenous to their respective areas, when treating their pollen-sensitive patients.

F.W.W.

Proteins in Soy Milk Approximate Utilization of Egg Protein

Investigations recently conducted at Wayne University in Detroit have shown the soy proteins in Mull-Soy to have an average true digestibility of 89.6 per cent and an average biological value for maintenance of 95.6 per cent, compared with egg protein as 100 per cent.

The findings of this study using adult human subjects were published in a recent issue of the *Journal of Nutrition*, 28:209, 1944. The method of Murlin and associates was used to determine biological values.

Mull-Soy, a product of The Prescription Products Division of the Borden Company, has been used extensively for infant feeding, and also for children and adults, as a palatable, well-tolerated and easy-to-digest milk substitute.

PROGRESS IN ALLERGY

(Continued from Page 86)

Human Plasma and Serum Toxicity. State, David, and Levine, Milton: J. Lab. & Clin. Med., 28:1786, 1943. Reviewed in Ann. Allergy, 2:66, 1944.

Palindromic Rheumatism. Hench, P. S., and Rosenberg, E. F.: Arch. Int. Med., 73:293, 1944. Reviewed in Ann. Allergy, 2:456, 1944.

On the Anaphylactic Nature of Rheumatic Pneumonitis. Rich, A. R., and Gregory, J. E.: Bull. Johns Hopkins Hosp., 73:465, 1943.

By comparing the peculiar lesions of rheumatic pneumonitis with those of pneumonitis seen in sulfonamide hypersensitivity, the authors show them to be basically identical. Both types of pneumonitis demonstrate capillary damage characteristic of anaphylactic reactions. The authors present these findings, therefore, as further evidence that the lesions of acute rheumatic fever may be anaphylactic in origin.

Allergic Reaction to Dried Human Plasma. Colonnell, William J.: U. S. Naval Med. Bull., 41:1356, 1943.

Angioneurotic edema, asthma and urticaria occurring in a patient transfused with blood plasma after having had two previous whole blood transfusions from the same donor is reported. Urticaria occurred following the second transfusion. There was no family or personal history of allergy. After reaction, the patient was found to be ragweed-sensitive (three plus), also one plus to same activated plasma (Dil. 1-10) that was used in transfusion. The donor was ragweed-pollen-sensitive. Ragweed allergen in pooled human plasma was demonstrated by passive transfer on three controls.